Clinical Medicine

Original Articles for November, 1959

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Clinical Medicine

Vol. VI, No. 11

CONTENTS FOR NOVEMBER, 1959

Editorial

Original Articles

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The reliable progestational activity of Enovid has been found highly valuable in controlling such uterine dysfunctions[1-6] as amenorrhea, menorrhagia and metrorrhagia. By stimulating and supporting the endometrium, Enovid establishes the regular proliferative, secretory and, on withdrawal, menstrual phases of the uterine cycle.

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Research in the Service of Medicine

CHICAGO 80, ILLINOIS

1. Kistner, R. W.: Conservative Treatment of Endometriosis, Postgrad. Med. 24:505 (Nov.) 1958. 2. Southam, A. L.: Symposium on Enovid: Clinical Application of Enovid and Other Progestational Agents in Control of Menstrual Disorders, Chicago, Searle Research Laboratories, 1959, pp. 11-14. 3. Roland, M.: Effects of Norethynodrel on the Human Endometrium, Ann. New York Acad. Sc. 71:638 (July 30) 1958. 4. Kupperman, H. S., and Epstein, J. A.: A Symposium on 19-Nor Progestational Steroids: Gonadotropic-Inhibiting and Uteratropic Effects of Enovid, Chicago, Searle Research Laboratories, 1957, pp. 32-45. 5. Weinberg, C. H.: Symposium on Enovid: Enovid for Relief of Dysmenorrhea and Control of Dysfunctional Bleeding and Endometriosis, Chicago, Searle Research Laboratories, 1959, pp. 19-24. 6. Greenblatt, R. B.: Symposium on Enovid: Progesterone and Progestins: Their Limitations and Comparative Values, Chicago, Searle Research Laboratories, 1959, pp. 4-10.

TABLE OF CONTENTS *(Continued)*

Original Articles

Case Report

Current Literature

In the Treatment of Rheumatic Disorders
Greater stability of maintenance dosage minimizes risks of hormonal imbalance

In Sterazolidin, the anti-inflammatory actions of prednisone and Butazolidi are combined to permit lower effective dosage of each. Clinical experien has indicated that patients can be well maintained on this combination o prolonged periods with relatively low, stable dosage levels of each compone thus minimizing the problems arising from excessively high doses of co costeroids. Other side effects have also been gratifyingly few. Antacid a spasmolytic components are contained in Sterazolidin capsules for the ben of patients with gastric sensitivity.

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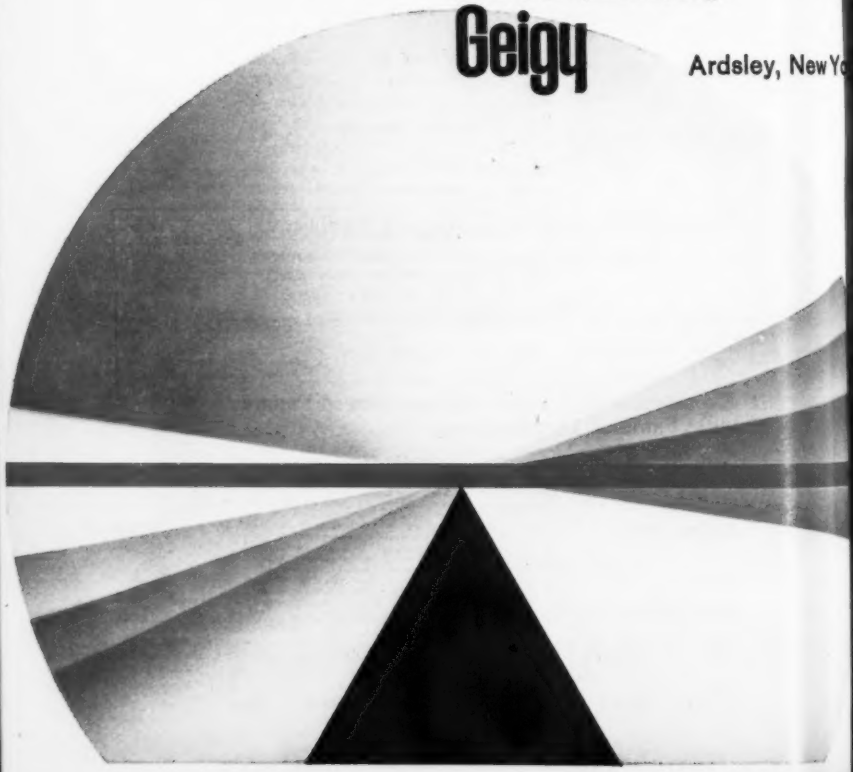

TABLE OF CONTENTS *(Continued)*

Current Literature

Briefs: Medical

Briefs: Surgical

TABLE OF CONTENTS *(Continued)*

Briefs: Therapeutic

Briefs: Dermatologic

Briefs: Pediatric

Briefs: Gynecologic

TABLE OF CONTENTS *(Continued)*

Briefs: Ophthalmologic

Departments

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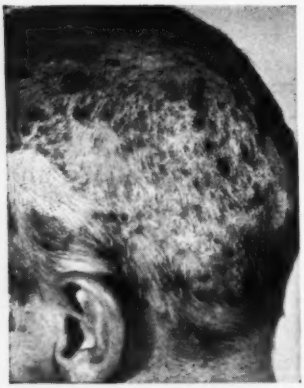

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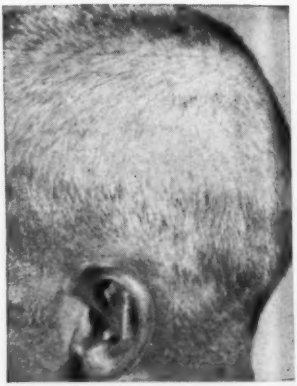

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EDITORIAL

On Oopherectomy

This surgical procedure should not be performed until the possibility of malignancy and endocrine imbalance have been evaluated

JAMES M. NORTHINGTON, M.D., *Editor-in-Chief*

My teacher of gynecology was that master surgeon, Dr. George Ben Johnston, one-time president of the American Surgical Association, and the first surgeon to perform an operation under "Listerism" in the Commonwealth of Virginia. In season and out of season Dr. Johnston told his students in lecture hall and surgical amphitheatre "The deepest Hell is for men who spay women." In medical meetings, county, state, regional, national and international, he condemned the removal of any ovary not cancerous.

Over the 50 years and more since I came directly under his teachings, I have gone along thinking that, almost universally, surgeons had espoused and were applying this principle.

Apparently this is not true, as I gather from an excellent article by Griffith.[1] Gynecologist Griffith's views and practice would delight the heart of my old professor to learn that there are still surgeons, and not a few, who are qualifying themselves for that deepest Hell.

Whether or not to remove normal ovaries at the time of hysterectomy for a non-malignant uterine lesion revolves mainly about our fear of future development of cancer of the ovary, an occurrence of such frequency and with so unfavorable a prognosis that some justification for

1. Griffith, G. C., *Obst. & Gynec.*, 7:479,1956.

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*Swartz, H.: To be published.

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the procedure might be made.

Certainly in young women this additional procedure is generally not advisable, but during the climacteric the procedure would seem to have some merit. Probably almost anyone who has seen ovarian cancer in patients who have had hysterectomy, patients who might have been spared this fate if the ovaries had been removed at the same operation, would be easily convinced that oophorectomy is advisable.

With the death rate of 20 per 100,000 in women 45 to 64, we might prevent two cases of ovarian cancer for every 10,000 operations if all of this age were castrated. In one report it is stated, "The fact remains that the incidence of patients in the series of 2,097 who developed carcinoma after having had initial surgery at the age of 40 or over, was 3.05%." To say that 3% of women with ovarian cancer have had operations at which oophorectomy would have prevented the disease, is far from saying that 3% of women with hysterectomy will have cancer of the ovary. None of the reports state the number of women who have had hysterectomy, nor do they list the indications for the operation. The conditions which produce the initial "benign" uterine lesion may have continued to act unfavorably on the ovaries or uterine activity before hysterectomy may have inhibited ovarian disease which afterward could proceed unchecked.

There can be no question that removal of healthy ovaries will usually prevent ovarian cancer, but whether by removing such ovaries some other metabolic disease may be precipitated is a matter worthy of consideration. To remove ovaries at the time of operation in women beyond a certain age is to perform this major surgical operation on the false assumption that chronological age and physiological age are one.

Proponents of removing ovaries say menopausal symptoms which may ensue can be adequately controlled with preparations now available. Control of symptoms is a far cry from restoration of endocrine balance. Menopausal symptoms occur in 25% of women after hysterectomy when ovaries are left intact.

It does not follow that the ovaries have ceased to function. The osteoporotic changes which occur in oophorectomized patients are noteworthy. According to Griffith, the deleterious effects on the cardiovascular system outweigh possible benefit from castration except in rare circumstances.

A patient far past the menopause may need her ovaries intact; one under 40 may need them removed. No patient who fears loss of libido should have oophorectomy, except in case of clear-cut necessity, regardless of age. The patient with cancerphobia or a family history of cancer should have oophorectomy regardless of age.

The term *routine*, applied either to conservation or to removal of ovaries, has no place in our present policy on hysterectomy for non-malignant disorders. The most favorable results will probably be achieved by pondering the merits of the procedure in each case.◀

ORIGINAL ARTICLE

Rehabilitation of the Rheumatoid Patient By Use of a Steroid-Relaxant Tablet and Physical Medicine

Recognition of the importance of physical therapy in the rehabilitation program will greatly improve prognosis

DOMINIC A. DONIO, M.D.,* *Allentown, Pennsylvania*

NEGLECTED TREATMENT

Physical medicine has a place of great importance in the rehabilitation of the rheumatoid arthritis patient, yet it continues as the most neglected approach of proved value in salvaging many arthritis patients from invalidism. Physical therapy has been shown to be most useful in the rehabilitation of the rheumatoid arthritis patient.[1-3] This demonstration seems to have been missed or ignored by many clinicians who would look upon this therapy adjunct as, at best, empirical.

Rheumatoid arthritis, of all the arthritides, presents the most serious problems diagnostically and therapeutically. No specific etiologic factor has been identified, and the plethora of possible factors must leave much

*Director of Physical Medicine and Rehabilitation Sacred Heart Hospital.

1. Rusk, H. A., *J. Nat. M.A.*, 45:1,1953.
2. Kessler, H. H., Rehabilitation of the Physically Handicapped, Columbia Univ. Press, New York, 1951.
3. Krusen, F. H., Physical Medicine and Rehabilitation for the Clinician, W. B. Saunders Co., Philadelphia, 1951.

to surmise as to prognosis and therapy.

Although the problems presented are difficult, there is a positive approach which will yield great profits in comfort and restoration of function. The physician who knows his patients and appreciates the nature of the disease, plus the capacities of the treatment and the precise time in which it should be used, can anticipate good therapeutic results. Our approach to the rehabilitation of the rheumatoid arthritis patient is based on the concept that whatever affects a part affects the whole individual. All too frequently alterations in joint function distract the physician's as well as the patient's attention from the consideration of other changes going on in the body. As a result, treatment is more or less limited to the use of gold salts, steroids, and other agencies directed toward the relief of joint symptoms.[4] Bony and cartilaginous changes are not the cause of deformity, changes in the periarticular soft tissues, muscles, tendons, fascia and skin having been shown to be more important.[5] The alterations in these tissues are amenable to corrective measures.

Before the proper program can be devised many aspects of the patient and his problems must be studied and evaluated.[6] An adequate rehabilitation program can be formulated only if the assets and deficits are determined in respect to the patient's general medical condition and functional capacity, as well as his psychosocial, vocational and economic status.[7] The proper prescription for the patient should include the balancing of physiological assets and liabilities resulting from the specific effects of the disease, the general response of the body function, and the effects of treatment procedures. It would be incorrect to indicate that this can always be achieved. Such an accomplishment awaits much more extensive and elaborate application of physiological knowledge of the disease state.[8] Treatment should make use of special diets, drugs, physical measures—cold, heat, rest, passive or active traction, and movement, in any combination—and surgical procedures as may be definitely indicated.[9]

4. Donio, D. A., *Clin. Med.*, 3:207,1956.
5. Preston, R. L., *New York J. Med.*, 55:2887,1955.
6. Donio, D. A., *Med. Times*, 84:1042,1956.
7. Rae, J. W., Jr., & Bender, L. F., *J.A.M.A.*, 160: 611,1956.

AIMS OF TREATMENT

The desire of the patient and the objective of the physician are to reestablish patient status, economically and socially, emphasizing the abilities and capacities of the patient, developing these abilities to their greatest possible use, and placing less stress on the inevitable disability.[10] Conservative treatment based on sound judgment is essential in the management of rheumatoid arthritis. We cannot sit by and entertain the patient while Nature struggles to effect improvement in his condition. It has been observed that the patient's desire to get well is the crux of a successful therapeutic program.[11] Good general health must be restored and maintained. Until a specific cure is discovered, different from anything available as of now, treatment must be based upon the physician's own broad experience.

DETAILED CASE-TAKING

A complete history with dietary

8. Spencer, W. A., *Phys. Therapy Rev.*, 34:61,1954.
9. Jones, A. C., *Arch. Phys. Med.*, 37:647,1956.
10. Rusk, H. A., New Hope for the Handicapped. The Rehabilitation of the Disabled from Bed to Job. Harper & Bros., New York, 1949.
11. Warter, P. J., *J.M. Soc. New Jersey*, 53:407,1956.

survey may supply clues of importance in prescribing treatment. Laboratory data are analyzed and x-rays are reviewed. A complete physical examination is carried out in each case. Then a program, individualized to the patient's status, is established. An assessment of the patient's functional capacity is made, so that some idea of possible rehabilitation can be arrived at, and a course of physical therapy charted. It is of extreme importance to give attention to the psyche in every patient.

SYSTEMIC DISEASE WITH LOCAL MANIFESTATION

Since rheumatoid arthritis is a systemic disease, rest is a basis for sound treatment, and it should be of such type and duration as to accelerate return to a state of health. Rest should be combined with the performance of general bodily exercises designed to maintain the functional integrity of the main muscle groups of the torso, as well as those of the limbs.[12] When the constitutional symptoms are severe and the affected joints are swollen, painful and in spasm, strict bed rest is the first consideration. With the patient at bed rest, all joints must be checked for good postural alignment. Periods of prone and supine positions are arranged. General rest for the patient does not contraindicate an active physical therapeutic program, even though the disease is acute as indicated by clinical and laboratory examination, since care at this time may play a large part in the extent to which the patient can be rehabilitated.[13] Physical therapeutic measures should cause a feeling of well-being. Rest should be obtained in an atmosphere free of any factors giving rise to apprehension and anxiety tension states.

12. Copeman, W. S. C., *Brit. M.J.*, 1:1185,1952.
13. Baker, F., *Bull. Rheumat. Dis.*, 4:57,1953.

FRAGILITY OF THE CAPILLARIES

The frequent occurrence of abnormal capillary fragility in rheumatoid arthritis has been observed.[14] A majority of patients exhibiting severe capillary fragility have been shown to be those with painful and swollen joints.[15] The capillary system plays a major role in the economy of the body, and thus deserves attention at all times. Management of arthritis is more effective in the presence of normal capillary resistance.[16] Abnormal capillary fragility and increased capillary permeability can often be corrected with hesperidin and ascorbic acid, each 100 mg., in capsule form.

GENERAL HEALTH CARE

Weight loss and anemia require attention. It may be necessary to give several blood transfusions, then continue with iron supplements and B_{12} with liver extract injections. The regular diet is supplemented with protein feeding in amount calculated on the requirement of the patient.

PSYCHIC FACTORS

The single constant in chronic arthritis is the disturbance of the psyche and "homeostasis,"[17] a word for the normal correlation and functioning of the different body systems, and the effect on these systems of emotions, particularly of rage and fear, acting via the endocrine glands. Anxiety tension and fatigue must be evaluated and attended to with diligence. Fatigue may be a preceding event in-

14. Warter, P. J., et al., *J.M. Soc. New Jersey*, 43:228, 1946.
15. Warter, P. J., et al., *Delaware M.J.*, 20:41,1948.
16. Warter, P. J., et al., *J. Am. Geriatrics Soc.*, 4:592, 1956.
17. Cannon, W. B., The Wisdom of the Body, W. W. Norton & Co., Inc., New York, 1932.

fluenced by the patient's occupation, his inability to adjust to environmental hazards, and his physical and neurological status.[11]

Control of anxiety tension state is an important objective throughout. A patient in a relaxed state is more amenable and in better condition to cooperate with the prescribed treatment.

THE AGENT GIVING BEST RESULTS

My choice as a muscle relaxant, tranquilizing and antirheumatic agent, is a drug combination containing 2.0 mg. prednisolone, 200 mg. of meprobamate, and 200 mg. of dried aluminum hydroxide gel.* This agent has been used over a period of 18 months with gratifying results and no side effects. The use of this steroid preparation affords rapid control of the various symptoms of rheumatoid arthritis, and is of great value in aiding the patient to obtain full benefit from a physical medicine and rehabilitation program. Pain guards against overuse of the affected parts. When pain interferes with proper rest, analgesics play an important role in the conservative treatment of the disease.[18] Our choice of analgesics continues to be aspirin. The anxiety tension state controlled, and the patient relaxed, various steroids for the anti-arthritic phase of our program were tried. For the past 18 months, I have used Meprolone, and found it muscle-relaxing, tranquilizing, and productive of anti-arthritic effects. Further experience has adequately supported our initial concept.

HOSPITAL CARE NOT NEEDED BY MAJORITY

Many of the procedures can be carried out in the physician's office or in the patient's home. It is important that the patient realize that the treatment must be planned for a long term and must be adhered to strictly. Heat, whether by the simple heating pad or the most elaborate diathermy machine, produces a definite physiological effect. It may relieve pain or relax muscles in spasm. Heat increases peripheral circulation, causes vasodilation, promotes healing of injured tissue, and permits mobilization of injured or diseased joints. Heat can be one of the most valuable agencies of office treatment.

PARAFFIN BATHS

Of the many methods of application of heat, the paraffin bath is my choice. Three or four pounds of paraffin are heated in the top of a double boiler until liquefied, a pint of mineral oil is added to lower the melting point. Then it is cooled until a thin white coating appears on the surface, when it is ready for use. Use of an inexpensive candy thermometer insures a proper temperature of the wax, usually 128 to 130° F.

Application to hands: Dip the hands in and out of the wax, keeping the fingers still, until several coatings are applied. Then allow the hands to remain in the wax 20 minutes. Remove the hands from the wax bath and let cool in toweling wrap; the wax can be peeled off easily and without discomfort.

Application to other parts: (knees, shoulder, elbow, back): Wrap several thicknesses of cloth around a wooden spoon and tie to make it secure. Dip into wax, and apply a coating over the entire area to be treated until completely covered. Apply 10 to 12 coatings, cover with a towel or blan-

*Meprolone®, Merck Sharp & Dohme, West Point, Pa.

18. Warter, P. J., *Med. Times*, 84:812,1956.

ket and leave on for 20 minutes. Peel off the paraffin and the part is ready for further treatment.

The use of hot packs is a good means of applying heat, easy, safe and inexpensive to use.

MODE OF ACTION OF HEAT

It is believed that heat accelerates the biochemical processes of the muscle, thereby favorably affecting the viscous and elastic properties of the contractile tissue. Because of the "soothing" effect resulting from heat application, there may be a tendency to its misuse by more frequent application, this doing more harm than good.

MASSAGE TOO LITTLE USED

It is regrettable that massage is so neglected. Maybe it is because it is time-consuming that it is pushed into the background. Proper massage sedates and relaxes, effects which should recommend it for more frequent use. If the massage is to be left to relatives, the physician should demonstrate and teach them the simple techniques. A light stroking up to, but not over, the affected joints, will benefit. Massage increases lymphatic circulation, relieves muscle spasm, and promotes local circulation.

Any physical activities or exercises must be within the tolerance of the patient. Their objective is to maintain or increase the strength, endurance, and coordination of muscles. An exercise program is probably the most important feature in the correction and prevention of deformities. Exercises, individualized for each patient, should be graded after proper testing of the patient's muscle power. The details should be explained to the patient plainly so as to gain his intelligent cooperation. Arthritic joints can be carried through a program of active, assistive-passive and resistive exercises. The pain in the joint determines the intensity of these exercises. Muscular exercises within the limits of tolerance are essential to reduce pain and muscle spasm, increase muscle power and restore normal rhythm of movement, and thus lessen the incidence of deformity.

Sufficient time should be allotted to the physical therapy program. Some of the techniques are time-consuming, but the time is usually well spent. Whatever program for home treatment is outlined, it should be administered at least three times each week. The prognosis of rehabilitation of a rheumatoid arthritis patient is good if the physical therapy program is well directed.

CONCLUSIONS

Experiences in the management of rheumatoid arthritis have demonstrated the value to rehabilitation of adequate medical treatment and a well-directed physical therapy program. The response of the patient to physical therapy will be enhanced if proper attention is given to the correction of capillary defects, the nutritional status, and the anxiety tension states.

Meprolone was of definite value in the medical management, conditioning and preparing the patient for his daily physical medicine program.

With adequate attention given these factors, and recognizing the importance of physical therapy in the rehabilitation program, the therapeutic profits in these cases will be greatly increased, and many patients will be saved from severe invalidism.◀

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1. English, A. R., and McBride, T. J.: Proc. Soc. Exper. Biol. & Med. 100:880 (Apr.) 1959. 2. Celmer, W. D.: Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959, p. 277. 3. English, A. R., and Fink, F. C.: Antibiotics & Chemother. 8:420 (Aug.) 1958.

ORIGINAL ARTICLE

Progress in Prostatic Surgery

Prostatectomy is now less formidable than it was previously, due to advances in technique and in combatting blood loss

J. ULLMAN REAVES, M.D.,* *Mobile, Alabama*

The step by step progress evolved in the suprapubic surgical approach to the removal of the prostate gland, from the time of Fuller and Freyer to the present, has saved a multitude of elderly men from suffering not to be estimated, and prolonged in usefulness and comfort the lives of thousands upon thousands.

The two most common causes of mortality and morbidity in suprapubic prostatectomy were blood losses and infection. Our advances in surgical technique together with the knowledge to combat blood losses has brought prostatectomy to a point where it is not near as formidable a procedure as it was 25 years ago. A complete physical examination after taking a detailed history will chart still further progress in dealing with the prostatic.

In 1899, in a case in which there was deep uremic coma and a hugely distended bladder, catheterization was attempted without success and suprapubic drainage was carried out. Young witnessed the amazing disappearance of the coma, and restoration of an apparently normal condition as a result of drainage. One month later, Young carried out his first suprapubic prostatectomy, removing a large prostate gland successfully through the previous cystotomy incision. This was the first recorded two-stage suprapubic

*The untimely death of Dr. Reaves occurred on September 19, 1959.

prostatectomy. The cystotomy wound was used to drain the bladder and regulate the blood chemistry to within normal limits. The suprapubic wound was either closed around a Marion drain that had a glass or metal piece which fitted into the protruding opening to facilitate urine drainage, or a pessary drain which was first straight and later made angular, so it would not pull against the wound. Keyes used a Marion drain following prostatectomy which had a lumen large enough to pass sponge forceps through to remove sizable clots. Stones if present were removed at the time of cystotomy, and digital exploration made of the viscus.

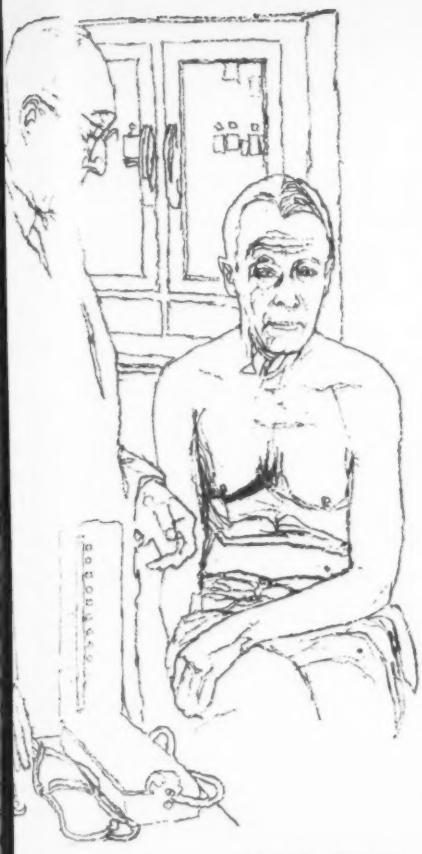
Pilcher introduced a bag having suprapubic and urethral attachments for urinary drainage into the prostatic cavity, inflated and made it taut by traction to control prostatic hemorrhage.

After the period of suprapubic drainage, Oswaldo Schwartz of Vienna reopened the suprapubic wound by blunt dissection and with a suture which was tied fast ligated the blood vessels just before they entered the prostate gland from either lateral angle of the trigone, following which he proceeded with the gland enucleation.

Harris presented his results of suprapubic prostatectomy with primary closure of the bladder. At this time Legue, of the Albarran Clinic in Paris, was doing suprapubic prostatectomies with perineal drainage. Later Rose, of St. Louis, did suprapubic prostatectomy with complete closure of the bladder without catheter drainage. With the onsweep of transurethral prostatectomy, the bladder drainage was accomplished by retention catheter until the blood chemistry was brought to within normal limits. This method became so helpful that it was carried out in one-step suprapubic prostatectomies, to establish drainage and regulate the blood chemistry.

The handling of post-surgical urinary outflow was now making step toward control, thus obviating and lessening fermentation with its disagreeable odor. This step was assisted by exhaust ventilation in some of the urological wards. The Foley bag catheter, with some modifications, was used extensively in drainage of the bladder following transurethral resection. Kretchmer continued to do cystotomy drainage prior to his prostatic resections. The prostatic cavity was packed with gauze wrung out in hot water, and most operators used considerable pressure which they thought aided in controlling hemorrhage. After this a bag catheter was passed through the urethra into the bladder, where the tip was pulled up, bag distended and oxycel gauze passed around the catheter ahead of the distended bag, so it would be pulled into the prostatic cavity and held there by the distended bag and traction of catheter distal to meatus. The traction on the distal end of the catheter, together with contraction of the fibers of the prostatic cavity served to break up the oxycel gauze, pushing many of the particles into the bladder some of which occluded the eyes of the catheter. This in some cases caused considerable soiling of the dressings and discomfort to the patient.

Infection was being combatted by sulfonamides and antibiotics as they made their rapid appearance from the drug houses. Great claims were made for the combatting of infection by these drugs singly and in combina-



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tion, best results being obtained when the surgery had established complete and free drainage. The incidence of secondary hemorrhage has slowly abated as methods of controlling the hemorrhage at the time of operation improved with the knowledge that the prostatic cavity contracts after removal of the gland in a manner similar to the action of the uterus after delivery of the placenta. Overdistention of the cavity, or too much pressure within, not only increases sepsis but may be a factor in causing excessive bleeding by preventing the normal contraction of the vesical neck and prostatic capsule.

In opening the bladder some classification of the classical midline incision is used. For the most part the patient comes to the operating table with a retention catheter *in situ*, and after the patient is prepared and draped, a sterile fluid is allowed to gravitate into the bladder through this indwelling catheter. A midline incision is made through the skin and fascia down to the musculature from the symphysis upward 5 or 6 cm. A slight Trendelenburg position is used if the patient has a pendulous abdomen. The muscles are separated in the midline by blunt dissection, and the exposed peritoneum is reflected upward, revealing the exterior of the anterior wall of the distended bladder. Further distention of the bladder is dispensed with. Using an 18 gauge hypodermic needle, a stab is made through the bladder wall in the midline of its superior exposed portion. Contents of the bladder flow through the lumen of this needle, after which it is removed. A guy suture of #1 catgut is now placed 1 cm. on either side of the midline of the bladder, the two tied singly, leaving two extremities 8 cm. in length which are tagged. Using these tagged sutures for slight traction, a stab wound is made with the point of the knife below the peritoneal fold with the edge of its blade toward the pubic crest. The edges of the wound are caught with Allis clamps, placing one blade within the viscus, the other without. Contents of the bladder are removed by expulsion and suction. The prostate is palpated and abnormalities sought.

After removal of the prostate by blunt dissection, the hemorrhage is controlled by placing hot compresses within the prostatic cavity. The topical application of the heat rather than deep pressure controls the hemorrhage, assisted by contraction of the prostatic capsule. A bladder retractor is placed in the suprapubic wound and the extent of the bleeding is visualized. If necessary, a hot pack is placed within the prostatic capsule, any bleeding area is grasped with artery forceps and ligated with a figure of eight suture. A 23 F. urethral catheter with a 30 cc. bag is placed through the urethra into the bladder. A 45 cc. Solusponge is next threaded over the catheter with the apex of the cone pointing distally to the meatus, the 30 cc. bag is inflated and the catheter pulled down. As the Solusponge enters the prostatic cavity it is held there by the inflated bag which prevents it from being expelled into the bladder, and keeps it in close apposition to the wall of the prostatic capsule as it contracts.

After careful inspection and exploration of the interior of the bladder, the retractor is removed. A 22 F. Foley catheter with a 5 cc. bag, inflated, is introduced within the bladder suprapubically, and allowed

to emerge from the superior angle of the wound. The incision is then closed around the catheter in two layers. A running suture of plain catgut is used for each layer, the second suture line catching the first so that no potential space for extravasation or infection between the bladder layers will exist.

A rubber-tissue drain is placed in the space of Retzius. The guy sutures are brought through the recti muscles and tied loosely, thus holding the bladder in close proximity to these muscles. The muscles are brought together with interrupted chromic gut, and the fascia is closed with running sutures of chromic gut. The skin is brought together with three or four sutures of black silk, and intervening gaping closed with skin clips. The wound is dressed and the patient sent to a recovery room, where through and through irrigation of sterile water or boric acid solution, 40 to 50 drops per minute, is started through the urethral catheter, to exit through the suprapubic catheter.

After transfer of the patient to his room the irrigation is reversed, entering the bladder through the suprapubic catheter and leaving by the urethral catheter. To facilitate the dissolving and evacuation of any clots which remain within the bladder at the end of 24 hours postoperatively, 1000 cc. of the irrigation fluid is allowed to flow through and through rapidly by way of the urethral catheter. This is followed by the rapid flowing of 500 cc. of fluid, this time entering through the suprapubic catheter. The dressings are not wet so are not molested. The bag of the suprapubic catheter is now deflated and the catheter removed. The rubber tissue drain is usually removed at this time. The patient is allowed to stand on his feet, and to take a few steps with assistance. Twenty cc. of the fluid is then removed from the bag of the urethral catheter. This catheter is strapped in at the end of 48 hours postoperatively, and the remaining 10 cc. of fluid removed from the catheter bag. The dressings have little or no soiling and are not disturbed until the fifth postoperative day, when they are changed at the time the skin clips and urethral catheter are removed. The patient begins to void and from that time the suprapubic drainage is slight or not at all.◀


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ORIGINAL ARTICLE

Clinical Report of Trifluoperazine, A Longer-Acting Phenothiazine

On this medication, 14 of 19 patients with acute anxiety reactions, and 14 of 19 schizophrenic patients were improved

RICHARD C. PROCTOR, M.D.,* *Winston-Salem, North Carolina*

The general practitioner can care for many mental patients. The medical profession is constantly being subjected to startling claims for new drugs and it is becoming more and more difficult to evaluate them clearly. The general practitioner is the first line of defense against mental illness and can, if he is interested enough to inform himself, handle many psychiatric patients at home, without having recourse to a psychiatrist or hospital. If the latter is necessary, early discharge of patients back to their community makes it essential that the local physician understand psychodynamic drugs. It is only through repeated clinical investigations with careful sifting of reports and intellectual honesty on the part of investigators, that we can discover the truly valuable medicaments.

*Assistant Professor of Psychiatry, Bowman Gray School of Medicine of Wake Forest College.

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Bibliography: 1. Parsons, W. B., Jr., and Flinn, J. H.: A.M.A. Arch. Int. Med. *103*:783, 1959. 2. Parsons, W. B., Jr., and Flinn, J. H.: J.A.M.A. *165*:234 (Sept. 21) 1957. 3. O'Reilly, P. O.: Canad. M. A. J. *78*:402 (March 15) 1958. 4. Altschul, R., and Hoffer, A.: Arch. Biochem. *73*:420, 1958. 5. Achor, R. W. P.; Berge, K. G.; Barker, N. W. and McKenzie, B. F.: Circulation *17*:497, 1958. 6. Altschul, R., and Hoffer, A.: Circulation *16*:499, 1957. 7. Hoffer, A., and Callbeck, M. J.: J. Ment. Sc. *103*:810, 1957. 8. Parsons, W. B., Jr., and Flinn, J. H.: Circulation *16*:499, 1957. 9. Achor, R. W. P., Berge, K. G.; Barker, N. W., and McKenzie, B. F.: Circulation *16*:499, 1957. 10. O'Reilly, P. O.; Demay, M., and Kotlowski, K.: Arch. Int. Med. *100*:797, 1957. 11. deSoldati, L.; Stritzler, G., and Balassanian, S.: Prensa méd. argent. *44*:3286 (Nov. 8) 1957. 12. Parsons, W. B., Jr., *et al.*: Proc. Staff Meet. Mayo Clin. *31*:377 (June 27) 1956. 13. Altschul, R; Hoffer, A., and Stephen, J. D.: Arch. Biochem. *54*:558, 1955. 14. Seebrell, W. H., and Harris, R. S.: The Vitamins; Chemistry, Physiology, Pathology. New York, Academic Press, 1954, vol. 2, p. 651. 15. Gregory, L.: J. Ment. Sc. *101*:85, 1955. 16. Sinclair, H. M.: Lancet *1*:381, 1956. 17. Page, I. H., *et al.*: J.A.M.A. *164*:2048 (Aug. 31) 1957. 18. Rosenfeld, L.: Am. J. Clin. Nutrition *5*:286, 1957.

RESULTS OF TRIFLUORPERAZINE THERAPY IN 50 PATIENTS

Diagnosis	Improved	Unimproved	Total
Anxiety reactions	14	5	19
Schizophrenia	14	5	19
Obsessive-compulsive behavior			
Depressive reactions	3	4	7
Totals	31	19	50

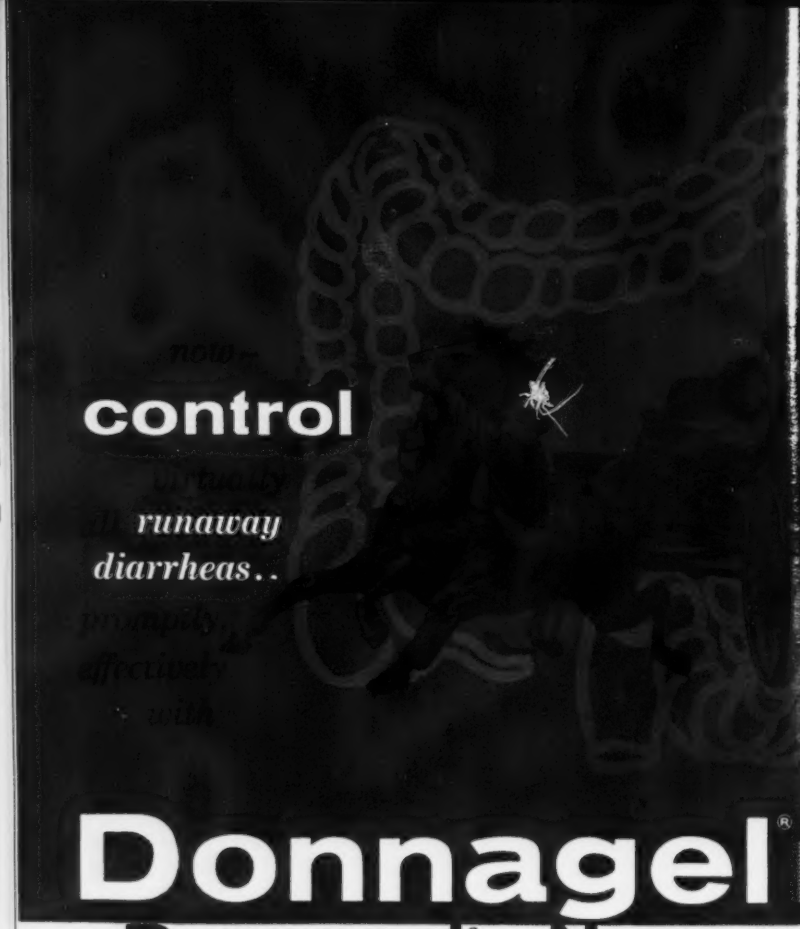
to warrant this report. The series of 29 females and 21 males were under the care of the author either directly or on a consulting basis.

Trifluoperazine appears to offer distinct advantages over other similar drugs. A high degree of effectiveness in schizophrenic patients who were withdrawn and apathetic was noted. It also proved valuable in chronically ill patients who had failed to respond to other therapy. Because of the potency of the compound there was a faster therapeutic response and, at the same time, lower dosage produced beneficial effect. It became evident soon after the clinical investigation was started that the medication had a longer period of activity than previously-used ataractic drugs, and that patients could be adequately maintained on doses twice a day rather than three or four times a day.

Many patients have failed to respond to previously available psychodynamic drugs or to the various types of shock therapy. Others, because of physical disabilities, have been considered poor risks for shock therapy. There are some patients who will fail to respond to this preparation, for no one drug brings symptomatic relief to all patients.

COMMENT

All schizophrenic patients were sufficiently ill to be hospitalized. They were grossly disturbed in thought and behavior. These patients were given no other form of somatic therapy while in the hospital other than the medication. They were started on 10 mg., three times daily; within three to five days. This was reduced to 10 mg. twice daily (morning and at bedtime). The patients who showed improvement began so to do within three days after the initiation of treatment. Most of the schizophrenic patients had previously been treated with other forms of somatic therapy —electroshock, insulin (both coma and sub-coma), and most of the newer drugs. Five patients with classical obsessive-compulsive disorders were treated without any improvement in symptoms. Three of seven patients who had manifested depressive reactions showed improvement. It is important to note that those who improved had an accompanying agitation while two who did not improve were agitated. The remaining two showed little or no agitation. It is also significant that none of these seven patients showed an increase or aggravation of their depressive symptoms. This may be significant in view of the fact that several psychodynamic drugs appear to aggravate depressions. Nineteen patients with moderately severe to severe anxiety were



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reated with doses of 10 to 15 mg. a ay. The results were very encouraging in that 14 of these patients showed mprovement in a short period of me. The study of the use of trifluoerazine in the treatment of psychoeurotics continues and will be reported later.

TWO OF PARTICULAR INTEREST

Two patients showed organic brain eterioration but are called "schizophrenics" for this study. One patient who had her first schizophrenic break t the age of 18 is now 38. She has been hospitalized nine times, and has received four courses of electroshock herapy for a total of over 100 treatments. She has had two courses of leep insulin coma and between the ast two hospitalizations had been on ne of the phenothiazine preparations. Clinically and on psychological esting she showed typical signs of rganic brain deterioration of a moderate degree. At the time of her last hospitalization she was started on rifluoperazine 5 mg. three times laily. At the time the medication was started she was severely agitated, restless, had marked insomnia and was suffering from paranoid delusions. Within three days she was more alm and relaxed, able to eat and leep and her delusions were less marked. Within a week the delusions had disappeared. She was discharged rom the hospital within a month and has now been at home for four months. She is taking the drug 5 mg. twice daily. There have been no unfoward effects and no toxicity has been noted. Since she returned home she has been keeping accounts and books for her father's various farming interests. In addition, she has been gathering material for a history of her home county which she is planning to write.

Another patient who has shown an even more dramatic response was first seen in 1956 at which time she was 52 years of age. At the age of 42 she had suffered a cerebral vascular accident with a partial right hemiparesis. Since that time her systolic blood pressure had varied from 230 to 150 and she had been on many different medications for this. For two years prior to being seen she had become progressively agitated, restless and depressed. She became suspicious, accused her husband of trying to get rid of her, etc. As the symptoms progressed, she felt people were talking about her, that the FBI was spying on her, that her house was "wired with microphones and cameras to catch me doing something." She was hospitalized and given seven electroshock treatments with marked improvement. Following her discharge she did well for six months, then began to be more quiet and spoke of thoughts of the death of her husband. She became quite paranoid toward her husband and son and suspected them of poisoning her food. She felt that her husband wanted to divorce her or get rid of her so that he could marry someone else. On readmission she was unkempt, her clothing disorderly. Blood pressure was 225/120. She showed a right hemiparesis with a deformity of the right foot and atrophy of the muscles of the right leg. Mental and psychological examination showed suspiciousness, paranoid ideation and signs of organic brain deterioration. She was treated with a low-salt diet, a general medical program (set up by a consultant in cardiology) psychotherapy and ataractic drugs. She improved suffi-

ciently to be discharged after four weeks of hospital treatment but had to be readmitted within a week because she had suffered a recurrence of the previous symptoms. She was started on trifluoperazine 10 mg. three times a day, along with her medical program for hypertension. Within a week the psychiatric symptoms had cleared and within two more weeks she was ready for discharge. She has been maintained at home for nearly three months and continues to be free of her paranoid delusions and ideations. She is cheerful, her affect is appropriate and normally labile, she is eating and sleeping well.

These two cases are presented as typical examples of those in which trifluoperazine is helpful. The rate of activity is rapid and the side effects minimal. For example, the sedation side effect is minimal. This drug is being used in low doses on patients suffering from anxiety who are employed in a local industry where manual dexterity and timing are important in the performance of their work. So far, it seems valuable in the symptomatic relief of anxiety without causing drowsiness or a "sedated" feeling. The results of this study will be more fully reported when it is completed.

Five of the 50 patients complained of transient dizziness and other symptoms of postural hypotension in the early stages of therapy. In all five patients this cleared within a week and in no patient was it necessary to discontinue the therapy because of this side effect.

Seven of the patients showed signs of extrapyramidal involvement of a mild degree on doses of 20 mg. a day or more. Four of these showed tremors only, and three showed tremors with rigidity. All of these cleared on reduction of the dose.

DISCUSSION

In general, trifluoperazine produced better results at lower doses than other phenothiazine derivatives. Tentative conclusions are that the therapeutic effect of this preparation on a dose schedule twice a day is similar to that from its administration three or four times a day. The onset of improvement is rapid and generally occurs within three days after the medication has been started. The incidence of side effects seems to be less when compared with the more frequent dose administration.

CONCLUSIONS

This is a report on a new compound which seems to offer promise of therapeutic efficacy and apparently warrants further clinical investigation. In a small series of patients suffering from chronic psychotic disorders, trifluoperazine produced improvement in a large percentage. The effective dosage is low—10 to 20 mg. a day; the activity is over a long period, so that a dosage schedule of twice a day is sufficient, the side effects are minimal and easily controlled. Of particular interest is the effect of the drug on two patients with a chronic brain syndrome who exhibited psychotic symptoms.◀

ORIGINAL ARTICLE

Chronic Interstitial Cystitis

Marked symptomatic relief has been achieved by instillation of a chlorine releasing solution into the bladder

GEORGE H. JONES, M.D., *Danville, Pennsylvania*

One of the most distressing problems facing the urologist during the past years has been that of chronic interstitial cystitis. The lesion frequently causing this problem is called "the vanishing ulcer of Hunner." When Dr. Hunner originally described this condition, he thought that the diagnosis of interstitial cystitis could not be made adequately unless such an ulcer could be demonstrated. The term "vanishing" applied to the ulcer merely indicates that it can appear on one cystoscopic examination, in a particular location in the bladder, and at a later date may have completely healed or may have changed its location to another part of the distensible portion of the bladder. It is well recognized today, however, that interstitial cystitis can exist without ulceration. The latter phenomenon occurs usually in the more acute phase of the advanced disease.

ETIOLOGY OBSECURE—MORBID ANATOMY VARIABLE

The cause of chronic interstitial cystitis is still not celar. Organisms which have been isolated by culture from bladder urine include B. proteus, E. coli and various forms of staphylococci; occasionally anaerobic organisms have been incriminated, and frequently sterile cultures are obtained. Interstitial cystitis must always be differentiated from tubercu-

lous infection of the bladder. Other names which have been advanced for this condition are pancystitis and panmural cystitis.

This chronic inflammatory process involves all layers of the bladder with monocytic infiltration of the mucosa, submucosa, muscularis and occasionally the serosal surface, so it is not surprising that there is a gradual contraction of the distensible portion of the bladder, with distressing symptoms of frequency of urination by day and by night, and suprapubic pain which usually indicates that ulceration of some type is occurring in the bladder. Some patients are barely able to leave the bathroom before they must return to pass a few more drops of urine. Gross bleeding is uncommon. Microscopic hematuria is frequently noted, particularly if the patient is suffering rather acute symptoms.

ALMOST EXCLUSIVELY AFFECTS WOMEN

Of 35 cases studied from March 1, 1955, to February 28, 1958, 34 were women. During the past 12 years this disease has been noted in males on only two other occasions. About 70% of females give a history of having had one or more previous pelvic surgical procedures. Whether or not this is a predisposing factor to limitation of bladder capacity by the institution of pericystitis is still not clearly known, however, clinical evidence lends support to this possibility.

DIAGNOSIS

The diagnosis of chronic interstitial cystitis is based upon the clinical history and particularly upon the cystoscopic findings. The most common symptoms are, in their order of frequency, nocturia, abdominal distress, urgency, burning, hematuria and low backache. These symptoms are always present to a certain degree, but frequently there are acute exacerbations during which time all the symptoms are greatly aggravated.

Urologic study by intravenous urography usually shows a normal upper urinary tract; in advanced cases there may be a certain amount of ureterectasis or even hydronephrosis resulting from ureteral obstruction at the ureterovesical junction.

Cystoscopic examination reveals the bladder mucosa to be pale and dull with increased vascular markings over the mucosa. If the bladder is examined during the very acute phase, ulcerations, stellate in type, are noted. These will frequently bleed freely when the bladder is distended, while the patient is under anesthesia. The presence of blood in the irrigating solution following overdistention of the bladder is considered a positive indication of interstitial cystitis, whether an ulcer can be demonstrated or not.

Treatment of this condition until relatively recently has been far from satisfactory. Bladder sedatives such as atropine, Banthine, Probanthine, local instillations of anesthetic solutions and periodic hydrostatic dilations of the bladder under anesthesia, have been well established during the past years. In very advanced cases in which symptoms are occurring every ten or fifteen minutes, urinary diversion has been carried out by ureterointestinal anastomosis of some type. Steroids have had a fair trial but have proven to be disappointing.

A NEW AND FAR MORE HELPFUL TREATMENT

Four years ago, clorpactin-WD-40, a solution which releases chlorine as

ts active ingredient, was found to give marked relief of symptoms when instilled into the bladder in proper concentration. With the advent of this drug, these unfortunate individuals have received a large measure of relief. Initially, it is preferable to instill the medication under anesthesia following a hydrostatic dilation of the bladder. The bladder, following the treatment, is placed at rest by indwelling catheter drainage for a period of 24 to 48 hours. If there is not prompt relief of symptoms following the removal of the catheter, a second hydrostatic dilation and instillation of clorpactin solution can be carried out. If, as is most common, the patient experiences considerable relief, the treatments are instituted on an outpatient basis with the instillation of either full-strength or a dilution of the clorpactin solution, depending upon how the patient tolerates it at intervals of three or four weeks.

ADJUVANT TREATMENT

In conjunction with the instillation, the patient is usually continued upon some type of relaxant, preferably Probanthine, Murel or Donnatal. Further treatment is carried out on an empirical basis. It depends entirely upon the patient's individual response as to the frequency of instillations, and even during a prolonged course of treatment it may be necessary from time to time to readmit the patient to the hospital for occasional hydrostatic dilation under anesthesia. This, however, is the exception, since some of the most severe cases seen during the past ten years have reached the point where they now prefer to come back for bladder treatment only if symptoms occur.

CONCLUSION

Although the action of clorpactin is still not clear, it can not be considered a curative agent, it remains today the best form of treatment available for this extremely distressing condition. Until the exact causative mechanism or organism can be identified and can be attacked directly, further treatment for chronic interstitial cystitis will have to remain empirical in nature. Clorpactin therapy to date has been highly successful in at least 95% of cases.◀

Tolbutamide: Evaluation in International Clinical Trials

In a total of 1,618 treated cases representing seven studies, the incidence of untoward side effects or toxicity was strikingly low. There was little significant hypoglycemia, a few instances of urticaria or skin rashes, some minor gastrointestinal disturbances, and one instance of duodenal ulcer with melena. Some patients manifested headache, muscular weakness, tingling, hemiparesis associated with hypoglycemia, transient alterations in the platelet count, and temporary reversal of the neutrophillymphocyte ratio (this in 37 of the 105 South African cases). There was one instance of severe leukopenia, resolving without alteration in dosage. Autopsy on two patients whose deaths were unrelated to the administration of tolbutamide revealed no pancreatic or hepatic damage attributable to the drug. The considerable variety of effects reported as due to tolbutamide administration prevents accurate determination of its toxicity.

Beckman, H., *Wisconsin M.J.*, 58:231-232,1959.

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ORIGINAL ARTICLE

Treatment of Resistant Staphylococcus and Hepatitis

Ultraviolet blood irradiation is presented as the treatment of choice for these disease conditions

R. C. OLNEY, M.D., *Lincoln, Nebraska*

Diseases due to staphylococcus infection and hepatitis are pathologic entities which differ greatly, and the methods of treatment thus far employed vary widely. They have one factor in common, *i.e.*, their resistance to antibiotic therapy. In both conditions the methods of treatment generally employed are ineffective, and the great increase in the incidence and severity of both conditions is alarming.

The Knott Technic of ultraviolet blood irradiation has been found to be effective in the treatment of severe staphylococcic infections, staphylococcemias, and viral and serum hepatitis. It is for this reason a summary of findings in the use of one therapy in the treatment of two widely varying pathologic states is presented.

RESISTANT STAPHYLOCOCCUS

The value of ultraviolet blood irradiation by the Knott Technic in the treatment of severe staphylococcic infection and staphylococcic septicemia has been proved over a period of many years. The significance of the results of this treatment as shown in these reports stands out clearly when compared with the many identical cases treated with other methods.

Twenty-four years ago observa-

tions were made of the effect of ultraviolet blood irradiation in treatment of patients with severe staphylococcic septicemia.[1] These patients recovered following three to five such treatments.

Patients with severe puerperal staphylococcic septicemia, including patients in moribund condition, recovered after ultraviolet blood irradiation treatments.[2]

In 1942, 103 cases of acute pyogenic infection were treated with the Knott Technic of ultraviolet blood irradiation.[3] At that time further studies were reported on the use of this irradiation in severe streptococcic and staphylococcic septicemias in postabortional sepsis, indicating prompt and effective control of the disease process.[4]

In 1943 a series of cases of severe peritonitis were treated successfully with this technic.[5] The same year the effective treatment of Escherichia coli septicemia by this method and the disappearance of hemolytic Staphylococcus aureus septicemia following ultraviolet blood irradiation were recorded.[6,7]

Further observations of the efficacy of the Knott Technic of ultraviolet blood irradiation therapy in the control of staphylococcemias were made in 1944.[8]

This impressive array of investigative work indicates the apparent value of this technic in the treatment of the most resistant forms of staphylococcus infection, in comparison with other methods.

1. Hancock, V. K., & Knott, E. K., *Northwest Med.*, 33:200,1934.
2. Rebbeck, E. W., *Am. J. Surg.*, 54:691,1941.
3. Miley, G., *New York J. Med.*, 42:?8-46.1942.
4. Rebbeck, E. W., *Am. J. Surg.*, 55:476-486.1942.
5. Miley, G. P., & Rebbeck, E. W., *Rev. Gastroenterol.*, 10:1-26,1943.
6. Rebbeck, E. W., *Arch. phys. Therap.*, 24:158-167&176.1943.
7. Miley, G. P., *Am. J. Surg.*, 62:241,1943.
8. Miley, G. P., *Am. J. Surg.*, 64:313,1944.

In the past ten years various antibiotics have been used extensively and effectively against most pyogenic organisms. From our knowledge of biology and biological reaction, however, it can logically be anticipated that organisms will develop a resistance to anything antagonistic to them which fails initially to destroy them completely. In many ways we are now confronted with the same problem we faced prior to the introduction of antibiotic therapy. This dilemma is further complicated by the fact that there are apparently some strains of staphylococcus resistant to all antibiotics. These strains are observed to be more virulent than previously, due to the antagonistic effect of antibiotics.

The mode of action of the Knott Technic differs completely from that of antibiotic therapy. While antibiotics attack the invading organisms, they do nothing to increase the resistance of patients against infection. The action of ultraviolet blood irradiation is to increase the resistance of the patient against infection, thus attacking the infection in the most biologically effective manner. By the increase in phagocytic action of white blood cells, increase of oxygen absorption, reduction of edema and decrease of toxic symptoms, the normal resistive forces of the patient are increased rapidly and effectively.

HEPATITIS

In the treatment of infectious and serum hepatitis, bed rest, protein diet and similar general measures constitute the accepted procedure. In these disease conditions the Knott Technic has proved to be the therapy of outstanding value.

A recent paper presented the find-

ngs of 16 collaborators covering observations over a period of nine years.[9] This work, carried on with meticulous care as to confirmation of diagnoses by laboratory studies, resulted in the following observations:

1. Of 43 patients with acute viral hepatitis treated with the Knott Technic, 31 had acute infectious hepatitis, three of long standing, and 12 had acute serum hepatitis.

2. An average of 3.28 treatments per patient was administered.

3. The average period of illness after institution of this therapy was 19.2 days. Clinical recovery was confirmed by laboratory studies.

4. Two recurrences were observed among the 43 patients treated during a follow-up period averaging 3.56 years.

5. No deaths occurred among these 43 patients.

6. A rapid subsidence of symptoms—nausea, vomiting, anorexia, pain and jaundice—was noted in all patients treated, as well as a coincident trend back to normal of laboratory findings. Marked improvement was noted in 27 patients within three days or less after institution of this therapy. Eleven patients showed marked improvement in four to seven days and five patients were markedly improved in eight to 14 days.

7. No untoward effects or unfavorable reactions were observed as the result of ultraviolet blood irradiation therapy in these patients, and no patient was found unable to tolerate the therapy. None developed a resistance to it.

CONCLUSIONS

It is believed that the Knott Technic irradiation therapy can promptly terminate an acute attack of viral hepatitis, prevent recurrences and arrest liver damage.

An increase of over 300 per cent in the incidence of viral hepatitis during 1951 to 1953 is indicated by the following figures furnished by the Department of Health, Education and Welfare, Public Health Service:

Cases Reported	
1951	7,349
1952	17,428
1953	33,382

The weekly report published by this same department lists a total of 6,463 cases of infectious and serum hepatitis reported during the first 19 weeks of 1958.

In the face of the growing problem presented by this disease and the lack of any other effective treatment for it, the results presented herein are considered significant.

SUMMARY

At this time ultraviolet blood irradiation by the Knott Technic stands out as the therapy which has proved, over years of time, to be of tremendous value in the treatment of two pathologic states known to resist other types of therapy, *i.e.*, severe staphylococcic infection, and viral and serum hepatitis, in both their acute and chronic stages. The great significance of the results of this treatment as shown in these reports stands out clearly when compared with the many identical cases treated with other methods.

There have been no untoward reactions to this therapy in over 800,000 treatments administered during the 25 year period of its use.◀

9. Olney, R. C., *Am. J. Surg.*, 90:402-409,1955.

ORIGINAL ARTICLE

Griseofulvin in Superficial Fungus Infections

Various cutaneous fungal disorders, some of up to 25 years' duration, were completely cured in 26 of 29 patients

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ORIGIN AND EARLY TRIALS

Griseofulvin†, an antifungal antibiotic effective against certain superficial fungus infections, was isolated[1] in 1939 from Penicillium griseofulvum dierckx; however, it failed to show antibacterial activity and was forgotten since antibiotic research at that time was primarily directed toward the discovery of antibacterial agents. In 1947 a substance was isolated from Penicillium janczewski, which was called the "curling factor" because its addition to fungus cultures resulted in abnormal development of fungal hyphae; they shriveled and became stunted.[2] Griseofulvin and the "curling factor" were later identified as the same substance.[3] Griseofulvin has also been isolated from Penicillium patulum. In succeeding years griseofulvin found wide application against fungal diseases in plants[4-9] as well as in veterinary medicine, where it was used in the treatment of ringworm in cattle.[10]

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†Griseofulvin for these studies was furnished as Fulvicin®, courtesy Schering Corporation, Bloomfield, N. J.

1. Oxford, A. E., et al., *Biochem. J.*, 33:240,1939.
2. Brian, P. W., Report Proc. Fourth Intern. Congr. Microbiol., 1947, pp. 153-154.
3. Grove, J. F., & McGowan, J. C., *Nature*, 160: 574,1947.
4. Stubbs, J., *Ann. Appl. Biol.*, 39:439,1952.
5. Brian, P. W., et al., *Nature*, 167:347,1951.
6. Brian, P. W., *Ann. Appl. Biol.*, 39:434,1952.
7. Aytoun, R. S. C., *Ann. Botan.*, 20:297,1956.
8. Goodman, R. N., *Plant Disease Reptr.*, 40:714, 1956.
9. Crowdy, S. H., et al., *J. Exper. Botany*, 7:42, 1956.
10. Lauder, I. M., & O'Sullivan, J. G., *Vet. Rec.*, 70: 949,1948.

USE IN HUMANS

In spite of its successful use in horticulture and veterinary medicine, several more years passed before the use of griseofulvin against human fungus infections was explored. The first breakthrough came largely through work in experimentally induced ringworm in guinea pigs, which demonstrated its potential value in the treatment of human dermatomycoses.[11] Later, fungistatic amounts of orally administered griseofulvin were recovered from the hair of guinea pigs.[12] These studies proved that the material was absorbed from the gastrointestinal tract and incorporated into newly growing cells of the skin, hair and nails, eventually reaching the keratin where it exerts its effect upon the fungi. These studies gave impetus to worldwide clinical investigations of griseofulvin.

EARLY SUCCESSES IN HUMAN INFECTIONS

The first of the reports on the successful use of griseofulvin in human subjects came from Austria, where 15 cases of infections by dermatophytes were eradicated by oral therapy with griseofulvin.[13] This initial group included three cases affecting the nails, two scalp infections, eight of hands and feet, and two infection of glabrous skin areas. This was quickly followed by reports from investigators throughout the world.[14-24]

11. Gentles, J. C., *Nature*, 182:476,1958.
12. Gentles, J. C., et al., *Nature*, 183:256,1959.
13. Riehl, G., Griseofulvin: an Orally Active Antibiotic. Read before the Austrian Dermatological Society, Vienna, Austria, Nov. 27, 1958.
14. Pardo-Castello, V., et al., *Boletin de la Sociedad Cubana de Dermatologia y Sifilografia*, 16:1,1959.
15. Williams, D. I., et al., *Lancet*, 2:1212,1958.
16. Blank, H., & Roth, F. J., Jr., *A.M.A. Arch. Dermat.*, 79:259,1959.
17. Reiss, F., *Medical Circle Bull.*, 6:9,1959.
18. Goldman, L., Initial Experiences with Griseofulvin, Read before the Cincinnati Dermatological Society, Cincinnati, Ohio, Feb. 11, 1959.
19. Sulzberger, M. B., & Baer, R. L., *Excerpta Medica*, 13:145,1959.

SPECTRUM OF ACTIVITY

Griseofulvin has proved almost uniformly efficacious against the group of superficial fungous conditions known as ringworm infections. These include tinea capitis (ringworm of the scalp), tinea barbae (tinea sycosis, barber's itch), tinea corporis (tinea circinata, tinea glabrosa), tinea cruris, tinea pedis (athlete's foot), and onychomycosis (tinea unguium). Griseofulvin exerts a fungistatic, not fungicidal, effect upon the causative microorganisms of these infections: Trichophyton mentagrophytes (gypseum), rubrum (purpureum), schoenleini, sulfureum, tonsurans, verrucosum, interdigitale and violaceum; Epidermophyton floccosum, and Microsporum audouini, canis (lanosum), and gypseum (fulvum). It has proved effective against these pathogens, regardless of the duration of the infection.

Griseofulvin has no effect upon moniliasis, cryptococcosis, sporotrichosis, North American blastomycosis, histoplasmosis, actinomycosis, coccidiodomycosis and chromoblastomycosis.[14,16,23] It is totally ineffective against bacteria.

Its effectiveness in tinea versicolor (pityriasis versicolor), an infection caused by Malassezia furfur (M. macfadyani, M. tropica or Microsporum furfur), is questionable. Complete failure in four cases of tinea versicolor has been reported by one worker,[16] however, another investi-

20. Robinson, H. M., Jr., et al., Griseofulvin, Clinical and Experimental Studies. Read before meeting of American Dermatological Assoc., Atantic City, N.J., June 4, 1959.
21. Pipkin, L., The Schoch Letter, May, 1959.
22. Griseofulvin: Dept. of Dermatology, Brooke Army Hospital, Fort Sam Houston, Texas, June, 1959.
23. Gonzales, Ochoa A., & Ahumada Padilla, M., Personal Clinical Observations. Read before the National Academy of Medicine, Mexico City, Mexico, March 18, 1959.
24. Sidi, E., & Spinasse, J. B., *La Presse Méd.*, 67: 1099,1959.

gator obtained rapid cures in two patients with the infection.[14] Encouraging results have been obtained with a topical form of griseofulvin in tinea versicolor.[25]

IMPORTANCE OF CORRECT DIAGNOSIS

The diagnosis of fungus infection cannot be made upon clinical impression only. Since numerous conditions, such as psoriasis, parapsoriasis, syphilis intertrigo, leprosy, seborrheic dermatitis, alopecias, a host of bacterial infections and moniliasis, may masquerade as those fungus conditions responsive to griseofulvin, diagnosis should in all cases be confirmed by appropriate laboratory studies. This is of particular importance in view of the seriousness of some of the unresponsive conditions. Prior to institution of treatment, scrapings should be taken from the marginal scales or a vesical top should be removed for examination. Part of this material is then used for direct mounting with a 20% KOH solution for the purpose of microscopic examination, and the remainder placed in a culture medium. When T. verrucosum is suspected, cultures should be enriched with thiamine and incubated at 37°C to allow the organism to grow better. Microscopic examination of hairs, scales, vesicle tops or nails will show the presence of fungi. In some cases, however, it may be difficult to culture the offending fungus and thus determine what species is responsible for the infection. While it is desirable to determine the species of fungus, patients in whom only the microscopic examination is positive should receive a trial of griseofulvin since, in the majority of such cases, the fungus present is one of those responsive to this antibiotic. The Wood's light is used in cases of tinea capitis, since hair infected with M. audouini or canis will fluoresce. Bluish-green fluorescence constitutes a positive diagnosis. Tinea capitis due to other fungi will not fluoresce under the Wood's light.

If local diagnostic facilities are not available, the clinician should send the scrapings to a medical mycology laboratory.

DOSAGE AND DURATION OF TREATMENT

The average dosage is 250 mg. four times a day. Children generally respond to one-half to three-quarters of the adult dosage. While early signs of response to griseofulvin, such as objective and subjective improvement of lesions of the glabrous skin, restoration of adequate perspiration and subsidence of itching, may be seen in the first few days, treatment should be continued for two weeks after both microscopic examinations and cultures prove totally negative for the presence of fungi, which may be recovered for some time after lesions have cleared.

Duration of treatment appears to vary according to the area of involvement. While some have reported cures of infections of the scalp and the glabrous skin in two weeks, three to 10 weeks are often required. Infections involving areas of thicker skin, such as the soles, usually require eight to 12 weeks, infections of the nails three to six months—some cases even longer. Toenails usually require somewhat longer therapy than fingernails.

SUPPLEMENTAL MEASURES

Since in tinea capitis the distal portion of the hair remains infected while the newly-growing hair is free from

25. Goldman, L., Personal communication to the author.

fungi, the hair is clipped close at weekly intervals. In cases of onychomycosis the nails should be kept short, but not surgically removed. Care should be taken to treat concomitant infections which may be unresponsive to griseofulvin.

Since fungi may remain viable under almost any conditions, infected gloves, hats, socks and stockings should be thoroughly decontaminated or discarded. The same is true of pillow cases and other objects that come into direct contact with infected areas of the patient.

POSSIBILITY OF DEVELOPMENT OF RESISTANCE

Although cases in which fungi have become resistant to griseofulvin have not been seen, it was recently reported that sensitive fungi may eventually develop resistance to griseofulvin in cultures.[20] We had one recurrence in a patient with a T. mentagrophytes infection of the toenails and soles which cleared completely upon retreatment—the original therapy may not have been continued for a sufficiently long period of time in this case. A case of a woman with T. rubrum infection, which relapsed several times after oral griseofulvin but can be maintained clear with topically applied griseofulvin, has been reported.[26] Repeated cultures from that patient showed the same degree of sensitivity to griseofulvin as the pretreatment cultures.

PRECAUTIONARY MEASURES AND SIDE EFFECTS

As with all new drugs, patients on griseofulvin are kept under rather close supervision. Blood counts are done at two-week intervals and patients are instructed to report immediately any abnormal manifestations, such as sore throat and fever. The only side effects observed in our series have been one instance of nausea and vomiting, which disappeared following reduction of dosage from 250 mg. q.i.d. to 250 mg. t.i.d., and two cases of apparently increased sun sensitivity. Undesirable effects observed by others include a few cases of drug rashes, urticarial, maculopapular or vesicular; occasional headaches,[19,23] and a case of reactivation of a long-standing colitis.[23] A few temporary white count depressions, which rebounded while the patients were still under treatment with griseofulvin, have been reported.[21] Although griseofulvin is obtained from three penicillia, there appears to be no cross-sensitivity with penicillin. Griseofulvin has been given to known penicillin reactors without untoward reactions.[16]

Some question has been raised as to the possibility of griseofulvin interfering with mitosis in actively dividing cells, particularly with spermatogenesis.[27] Such interference was observed in rats, following intravenous and intraperitoneal administration of unusually high doses (up to 200 mg./Kg.) of griseofulvin. These findings could not be confirmed in humans in whom periodic sperm counts were carried out.[16] A large-scale study involving weekly sperm counts as well as testicular biopsies in patients under long-term oral therapy with therapeutic doses of griseofulvin is now being conducted.[28] The results to date have shown no adverse effects upon spermatogenesis.

26. Goldman, L., Doctor-to-Doctor, Round-Table Conference on Griseofulvin, Atlantic City, N.J., June 4, 1959.
27. Paget, G. E., & Walpole, A. L., *Nature*, 182: 1320.1958.
28. MacLeod, J., & Nelson, W., Personal communication to the author.

AUTHOR'S SERIES

The series consisted of 50 patients (32 male and 18 female), aged 4 to 59 years (average 30 years), afflicted with a variety of cutaneous fungal disorders involving the scalp, axilla, extremities, groin, nails, lips, eyelids, neck, abdomen, chest, and face, for periods ranging from one day to 25 years (average 5 years). The offending pathogens, determined by culture and KOH slide, were T. rubrum in 27 patients, T. verrucosum in 15 (questionable in 3), M. audouini in 3, T. mentagrophytes in 1, E. floccosum (questionable) in 1, and M. canis (questionable) in 1. Initial dosage ranged from 125 mg. t.i.d. to 500 mg. q.i.d., in some cases reduced as the condition improved. The drug was employed for periods of from two weeks to six months, and at the time of this report is being continued in 23 of the patients, all with T. rubrum infections.

RESULTS

The 27 patients no longer receiving the drug are completely cleared and considered cured. The 23 patients still receiving the drug have all shown improvement since institution of therapy. The only side effects noted consisted of nausea and vomiting in one patient, which was stopped by reducing the dosage, and apparently increased sun sensitivity in two.

COMMENT

As indicated, there were 15 cases of infections due to *T. verrucosum*. This is a rather uncommon condition except in rural areas. *T. verrucosum* infection, usually is transmitted to humans by cattle, chiefly during the spring and early summer. Lesions may involve the beard, the scalp or other areas of the body; in our experience nails have not been affected. Unlike the other conditions responsive to griseofulvin, T. verrucosum infections are self-limited and will clear on an average of 6 weeks after reaching the pustular and granulomatous stage. The use of griseofulvin shortens the period of acute disability and may prevent the major scarring often seen. If therapy is started early during the circinata stage, the infection may be brought under control before reaching the granulomatous and scarring stage.

SUMMARY AND CONCLUSIONS

1. Griseofulvin has proved almost uniformly effective against the superficial fungus conditions known as ringworm infections, regardless of their duration.

2. Dosage for adults averages 250 mg. q.i.d. Children respond to one-half to three-quarters the adult dosage.

3. Duration of treatment varies from 3 to 6 months or more, depending upon the area of involvement.

4. Side effects appear to be rare and transitory. Apparently there is no cross-sensitivity between griseofulvin and penicillin. Development of resistance has not occurred in clinical studies to date.

5. Since many potentially serious conditions masquerade as tineas, diagnosis should be confirmed by laboratory procedures before treatment with griseofulvin is instituted.

6. Griseofulvin appears to be the first curative treatment for the hitherto virtually intractable superficial fungus infections.◀

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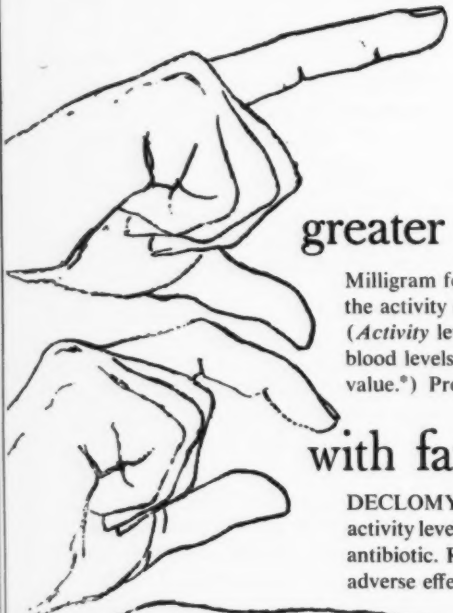

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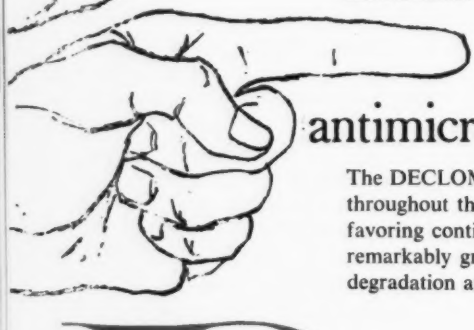

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*Hirsch, H. A., and Finland, *New England J. M* 260:1099 (May 28) 1

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ORIGINAL ARTICLE

Allergic Rhinitis: Symptomatic Treatment

A review of the etiology and symptomology of allergic rhinitis, with suggestions for treatment

JACK A. RUDOLPH, M.D., F.A.C.P., and
BURTON M. RUDOLPH, M.D., *Miami Shores, Florida*

Assuming that an accurate diagnosis of allergic rhinitis has been made and careful consideration given to the symptoms, nasal mucous membrane changes, cytology of the secretions, x-ray of the sinuses, the bacteriology, and the histopathology, the treatment must be of the total individual rather than limited to the specific etiologic excitants. The frequent complications and sequelae will prevent immediate cure in many cases. Treatment with drugs for temporary relief is necessary and often urgent.

SYMPTOMS

The symptoms to be considered in drug treatment are:

1. Post-nasal drip, often causing gagging and hawking in the early morning and even vomiting of mild to severe degree.

2. Pain, often severe enough to produce disability, is usually felt in the frontal area over the bridge of the nose, and may radiate to the temples or the back of the head. It is a dull, throbbing pain, often occurring each day at the same time and usually lasting two to four hours. Patients may complain of this pain only two or three times a week. This should not be confused with headaches of psychogenic origin.

3. Nasal obstruction is usually in-

termittent and often insidious, but may be acute and extreme. It may be bilateral or may alternate from side to side. Constant obstruction often leads to polyp formation.

4. Sinusitis is often suggested by the patient. Because of the frequently recurring "colds", the headaches, the feeling of fullness, the post-nasal drip and the profuse watery discharge, the patient's impression that he has sinusitis is magnified. There is a return of flakes of clear mucus in maxillary sinus irrigation. X-rays, transillumination and nasopharyngoscopic examinations often reveal normal sinuses. X-rays may show cloudiness due to mucosal thickening.

5. Instability, dizziness, or lightheadedness is often a feature, on bending or rising, but is not true vertigo.

6. Visual disturbances have been a complaint but no actual eye changes occur unless there is associated ocular allergy.

7. Emotions common to our daily living may be accentuated and may increase the allergic rhinitis. Globus hystericus may occur and be a confusing element. The persistent throat irritation may result in a choked feeling, shortness of breath and/or palpitations. This type of individual may begin to think he has carcinoma.

8. Chronic laryngeal irritation resulting from extension of the nasal symptoms may cause cough and hoarseness. From long standing irritation, laryngeal thickening and roughness may result. This process may involve the tracheobronchial tree, causing itching, cough and even spasm.

It is clear, therefore, that in the treatment of allergic rhinitis the total personality must be considered.

The palliative or symptomatic drug treatment of allergic rhinitis consists either of the internal administration of drugs or of their local application to the nose.

The most important drugs given internally are the many antihistaminics.

ANTIHISTAMINES

A practical means of trying out the antihistaminic compounds on the individual patient has been devised.[1] The compounds are divided into four groups, based on their formula similarities and similarity in clinical effectiveness.

For example, Benadryl and Decapryn may be classified as Group I; Pyribenzamine, Neohetramine, and Phenergan as Group II; Chlortrimeton and Pyronil as Group III; and Perazil and Antistine as Group IV.

SIDE EFFECTS

Gastro-intestinal upsets are not uncommon from members of Group II, so members of Group III or IV are preferable. Drowsiness is less frequent following ingestion of drugs in Group III, and also those in Group IV, so in persons having to work or drive an automobile, drugs in Group IV should be used first. It should not be assumed that no antihistaminic will relieve the symptoms of a patient until the compounds of each group have been tried.

Nearly all antihistaminics have a sedative action and all have an atropine-like affect.[2] Certain ones have greater effect in one respect than in others, e.g., Benadryl and Decapryn have a greater sedative action, Pyri-

1. Sheldon, J. M., et al., *Bull. Am. Soc. Hosp. Pharmacists*, 7:252,1950.
2. Sheldon, J. M., Panel Discussion on Allergy of American College of Physicians, April 16, 1953, Atlantic City, N. J.

benzamine and Neohetramine have a greater antihistaminic and antihyaluronidase effect. So the symptoms would determine what antihistamine may be selected.

EPHEDRINE

Either natural or synthetic ephedrine will often aid by reducing the nasal obstruction and its distressing symptoms. For the relief of the rhinorrhea, it may be combined with atropine or belladonna, or with sedatives to overcome the nervousness caused by ephedrine, and perhaps some of the nervous tensions incident to the attack.

ACTH AND STEROIDS

Corticotropin (ACTH) or the steroids (cortisone, hydrocortisone, prednisone, prednisolone, etc.) should be used only to relieve the most distressing symptoms after other treatment has failed, or as supplemental therapy in previously unsuccessfully managed seasonal nasal allergy. These hormones should not be used in the acute paroxysmal attacks since they do not work fast enough. ACTH and the steroids should not be prescribed lightly.

The newer steroids should be used with the same caution as the older preparations, for only experience gained with judicious trials will make more precise evaluation possible.

LOCAL MEASURES

Using sound physiologic principles, it is now possible to prescribe nasal medication that fulfills four cardinal requirements:

1. An isotonic aqueous solution compatible with ciliary action.

2. Normal, slightly acid, physiologic pH.

3. Non-injurious to nasal and sinus mucous membrane.

4. Free from local and systemic side effects.

Any break in the continuity of the mucous coating or interference with the action of the cilia permits the entrance of pathogenic organisms into the tissues. The natural defenses of the nose are necessary to the preservation of a normal, healthy state, and any nasal medicament employed should favor these defenses. Unless a solution applied to the tissues is isotonic with the tissue fluids, irritation and damage may result.[3] Cilia remain active for long periods in a physiologic solution of sodium chloride, but lose their activity with an increase in the sodium chloride to 4% or higher.[4] If the concentration of the solution is made hypotonic, all activity ceases and the cilia are permanently disabled. Investigations[5] have demonstrated the importance of the normal physiological reaction of the nasal mucosa. Drugs on the alkaline side may disturb the pH level of the clinically normal nose, irritate the mucous membrane, and postpone the return of the membrane from a pathologic alkaline state to one of normal slight acidity. Bacteria which cause or accompany acute infections secondary to allergic rhinitis find an alkaline field favorable for their growth. Any measure which supports or exaggerates this alkalinity favors the growth of bacteria and inhibits any natural healing process.

VASOCONSTRICTORS

During an attack of allergic rhinitis, use of a nasal vasoconstrictor that

3. Stark, W. B., *Arch. Otol.*, 8:47,1928.
4. Proetz, A. W., Essays on Applied Physiology of the Nose, Annals Publishing Company, St. Louis, 1941, p. 334.
5. Fabricant, N. D., *J. Am. M. Sc.*, 230:436-439, 1955.

brings the abnormal alkaline reaction to a normal or slightly acid reaction is therefore desirable.

THE BASAL CELLS AND THEIR CILIA

Ciliary activity can be easily impaired; its restitution is possible so long as the basal cells of the mucous membrane are not injured. Such cells can, however, be easily damaged by astringents, antiseptics or other cell poisons which contain protein-precipitating material. Markedly alkaline or markedly acid drugs are irritating and may cause irreparable damage to the mucous membrane. Some highly alkaline solutions of sodium salts of sulfonamides destroy the cilia[6] and disorganize the olfactory epithelium.[7,8]

Intelligently chosen nasal medicaments will relieve nasal congestion, maintain the normal function of the mucous membrane, and establish adequate drainage from the nasal sinuses, giving a reasonable measure of comfort without harming the nasal mucous membrane.

SUMMARY AND CONCLUSIONS

Allergic rhinitis designates a disease characterized by paroxysmal attacks of sneezing, nasal obstruction and serous discharge, usually of short duration, not accompanied by any of the constitutional symptoms of an infectious rhinitis, and generally not confined to any season of the year.

IS THE CONDITION ALTOGETHER OF ALLERGIC ORIGIN?

The basic question and consideration of greatest importance in determining treatment is whether the condition is entirely allergic. Many cases arise from non-specific irritation due to changes in temperature, irritating vapors, emotional stresses and fatigue. The reaction of the membrane may be divided into three stages:

1. Those which occur principally during the paroxysms of sneezing and affect primarily the secretory glands, causing discharge of a thin clear mucus, which after several days thickens.

2. The most common type, in which there is also intense nasal itchiness with paroxysms of sneezing followed by nasal obstruction, which may be as troublesome as the attacks of sneezing and may persist for several hours or days. The swelling may be due largely to rapid engorgement of the turbinates, which can disappear as suddenly as it came. Other possibilities are lachrymation and dryness and tickling of the naso-pharynx, along with irritation of the larynx, which can cause coughing.

3. Some patients are seen because of headaches, due to swelling of the sinus mucus membranes, others because of mental depression, lassitude, loss of the sense of smell, polyps, obstructing the eustachian tube with more or less loss of equilibrium.

CURATIVE TREATMENT

This is dependent upon the determination of the specific etiologic agent or agents, and is similar to that employed in asthma or other allergic conditions. Elimination or avoidance of antigens must be practiced when possible, hyposensitization if necessary. The judicious use of antihistamines or ephedrine is of value for symptomatic relief; steroids should be used only as a last resort and with caution.◀

6. Futch, C. E., et al., *J.A.M.A.*, 119:7,1942.
7. Hunnicutt, L. G., *Arch. Otol.*, 36:837,1942.
8. Fantus, B., General Technic of Medication. Third Edition, A.M.A., Chicago, 1938.

ORIGINAL ARTICLE

An Agent for the Symptomatic Relief of Migraine Attacks

Cyclizine hydrochloride, added to ergotamine tartrate and caffeine, appears to provide relief of migraine headache

ROBERT E. RYAN, M.D., *St. Louis, Missouri*

Of the various forms of vascular headache problems, the most commonly encountered by the practicing physician is migraine. Most likely the migraine-tension type of headache is the most frequently encountered type of vascular headache. It is estimated that 85 per cent of the cases of true migraine have some element of tension present.

RESEARCH IN THIS FIELD HAS BEEN PROFITABLE

The symptomatic treatment of migraine was, for a great many years, widely speculative. So great a number of preparations was presented in the medical literature as being successful that it would be impossible to mention them all. The vast majority of these preparations faded out of the picture soon after they were initially reported and have not since been heard of in the field of migraine therapy.

The tremendous amount of research into vascular headache, most of it into the symptomatic aspects of the migraine problem, has yielded spectacular results.

During the last few years, several new preparations have been used in the symptomatic treatment of mi-

graine and histaminic cephalalgia. These preparations are used primarily to abort the headache attacks.[1] All of the reports on drugs for the symptomatic treatment were consistent in one respect: all drugs produced some side effects of mild nature, and a certain number of cases would not respond. The percentage of failures varies with each individual agent.[1-6]

ERGOTAMINE AND CAFFEINE COMBINATIONS EFFECTIVE

The combination of ergotamine tartrate and caffeine appears to be of great value when used to abort attacks of migraine headache. When this combination of drugs is used, most of the reports in the medical literature show that 10 to 15 per cent of the patients experience some toxic side effects, usually of the gastrointestinal type—nausea, vomiting, and/or abdominal cramps. Even in the early research describing the relief obtained from the headache of migraine attacks by using the combination of ergotamine tartrate and caffeine, a large percentage of gastric side effects were reported.[1] So while the combination of these two drugs seems to be very helpful in bringing about relief from the typical migraine headache, any new combination of drugs which will cut down these gastric side effects and still give the patient relief from his headache would be a long step forward.

THE NATURE OF THE NEED FOR AN AGENT AFFORDING IMPROVED RESULTS

The pain of a typical migraine attack is of a throbbing nature and is more or less periodic, usually lasting for several hours or perhaps for several days. The migraine headache is usually hemicranial, usually associated with nausea, vomiting, scotomata, photophobia and a family history of similar headaches. Migraine headaches appear in women more often than in men in a ratio of more than two to one. In women, the attacks are often more severe at the start and during menstruation. These patients usually state that their attacks are "sick headaches." Continued research is being made in the field of the migraine type of vascular headache for a preparation which will prevent or may be depended on to abort the headache attacks, with the production of few or no side effects.

The subject of this study is a preparation composed of ergotamine tartrate, caffeine, and cyclizine hydrochloride.* It is widely accepted that ergotamine tartrate and its derivatives have been found superior to other types of drugs which are used to abort attacks of migraine. Ergotamine tartrate is considered by many physicians as being a specific agent for the symptomatic treatment of migraine attacks. Ergotamine diminishes the intensity of the migraine attacks by reducing the amplitude of pulsations of branches of the carotid artery.[7]

Caffeine has been found to increase the effectiveness of ergotamine tartrate. This is apparently due to the constriction of cerebral blood vessels and the reduction of the cerebral blood flow. Caffeine is a central stimulant, whereas the ergotamine tartrate is a sympathetic sedative. It

1. Horton, B. T., et al., *Proc. Staff Mayo Clin.*, 5: 105-108,1948.
2. Ryan, R. E., *Postgrad. Med.*, 5:330,1949.
3. Ryan, R. E., *J. Missouri M.A.*, 47:107,1950.
4. Horton, B. T., et al., *Proc. Central Soc. Clin. Res.*, 15:91,1942.
5. Peters, G. A., & Zeller, W. W., *Proc. Staff Meet. Mayo Clin.*, 24:565-568,1949.
6. Ryan, R. E., *Missouri M.J.*, 281-283,1955.

*Migral®, Burroughs-Wellcome & Co., Inc., Tuckahoe, New York.

7. Graham, J. R., & Wolff, H. G., *Proc. A. Res. Nerv. & Ment. Dis.*, 18:638,1937.

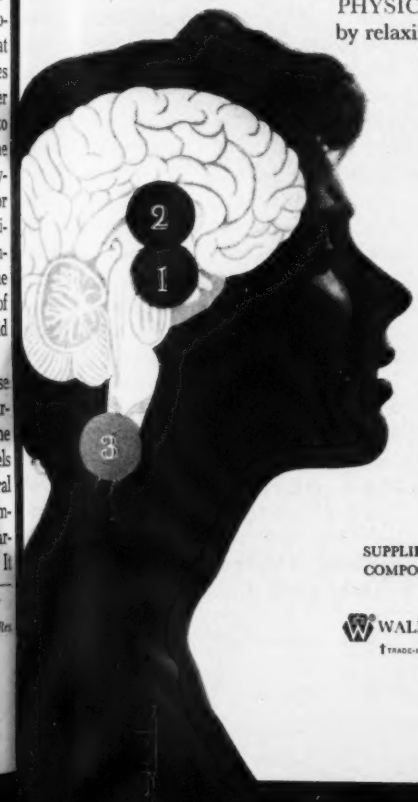
COMPREHENSIVE, THREE-LEVEL TREATMENT OF DEPRESSION

AND ASSOCIATED ANXIETY AND PHYSICAL TENSION

RELIEVES DEPRESSION
including symptoms such as crying, lethargy, loss of appetite, insomnia

RELIEVES ASSOCIATED ANXIETY
with no risk of drug-induced depression

RELIEVES ASSOCIATED PHYSICAL TENSION
by relaxing skeletal muscle



1
hypothalamus

2
thalamus and limbic system

3
spinal cord

▲Deprol▲†

benactyzine + meprobamate

- confirmed efficacy
- documented safety

SUPPLIED: Bottles of 50 light-pink, scored tablets
COMPOSITION: Each tablet contains 1 mg. benactyzine HCl and 400 mg. meprobamate

WALLACE LABORATORIES • *New Brunswick, N. J.*

†TRADE-MARK

09-9290

has been found also, that when caffeine is added to ergotamine tartrate, the effective dosage of the ergotamine can be greatly reduced, probably because of an increase in the rapidity of the absorption of the ergot.[8]

MAIN OBJECTIVE

The addition of cyclizine hydrochloride* to the already effective combination of ergotamine tartrate and caffeine was made in an attempt to reduce the number and severity of gastric side effects produced by the use of this combination. Cyclizine hydrochloride has been proved to be effective in reducing nausea and vomiting of other causation.[9,10]

THE ACCOMPLISHMENT

This drug belongs to the antihistamine group, and it might be expected therefore to produce drowsiness. However, since migraine has some element of tension, this mild sedative action is in most cases desirable. The fact that the addition of cyclizine hydrochloride to the other two remedial agents has improved the efficacy of the drug combination may be due largely to this sedative action.

Nausea and vomiting usually are prominent symptoms of migraine, so if the ergotamine and caffeine can either produce or increase the gastric side effects which are already present, the patient will be fearful of taking such medication. Therefore, if the addition of cyclizine hydrochloride counteracts this, and cuts down on the gastric symptoms already present, this is a step onward in the symptomatic treatment of migraine.

Cyclizine was found to block the vagus responses, and to relax the tone and the rhythmic contractions of the ileum.[11] This drug has an anticholinergic and an antihistaminic action, both of which tend to calm the gastrointestinal tract. Part of its action is believed to be mediated through the chemoceptive trigger zone outside the vomiting center. This suggests why the drug is useful against drug-induced nausea, since this type of nausea is usually mediated through this zone.

No influence, apparently, was exerted on blood pressure, pulse, respiration, hemopoietic system, kidneys, or liver function. Its only side effect is drowsiness, in migraine problems an action more favorable than not.

A THERAPEUTIC COMBINATION

The preparation is composed of 1.0 mg. ergotamine tartrate, 50.0 mg. caffeine, and 25.0 mg. cyclizine hydrochloride. The best dosage seems to be two tablets, given at the onset of the headache attack. The patient must be instructed to always have the tablets with him and to take two of them at the first premonition of an attack. A third tablet may be taken 30 to 45 minutes after the initial dose, if the first two tablets do not completely abort, and merely dull, the headache.

Table 1 shows that if the patient takes the medication as described, the results will usually be satisfactory. It appeared to be completely successful in 70 per cent of the cases in which it was used to abort the attacks of a typical case of migraine headache, partially successful in another 20 per cent of the cases. *Migral* therefore produced complete or partial relief from the migraine attack in 90 per cent of the cases.

Only two of the 120 patients ex-

*Marazine®, Burroughs-Wellcome & Co., Inc., Tuckahoe, New York.

8. Friedman, A. P., *Am. Pract.*, 1:948,1950.
9. Moore, D. C., et al., *Anesthesiology*, 17:690,1956.
10. Dent, S. J., et al., *Anesthesiology*, 16:564,1955.
11. Norton, S., et al., *J. Pharmacol. & Exper. Therap.*, 112:297-305,1954.

ore satisfying sleep for more patients

len offers sound, restful sleep for patients who are sensitive to barbiturates, eld-atients, patients with low vital capacity and poor respiratory reserve and those are unable to use barbiturates because of hepatic or renal disease. Onset of with Doriden is smooth and gradual, usually with no preliminary excitation. len acts within 30 minutes, and sleep lasts for 4 to 8 hours. Except in rare cases, angover" or "fog," because Doriden is rapidly metabo-

SUPPLIED: *Tablets,* 0.5 Gm., 0.25 Gm. and 0.125 Gm.

Doriden
(glutethimide CIBA)

CIBA
SUMMIT N. J.

TABLE 1

RESULTS OF MIGRAL THERAPY OF MIGRAINE HEADACHE

No. of Patients	Excellent[1]	Good[2]	Poor[3]	Gastric Side Effects	Sedative Side Effects
120	84	24	12	2	18

1. Excellent-Complete relief; 2. Good-Partial relief; 3. Poor-No relief.

perienced gastric side effects, a considerable decrease from the number before cyclizine hydrochloride was added. Sedative side effects of a very mild nature were observed in only 15 per cent of the cases, and in cases of excessive tension this was usually a welcome effect. Some patients would be forced to take a short sleep. Awakening, they would find themselves completely free from their headache attack. The degree of sedation varies in direct proportion to the size and body weight of the patient and is usually so mild that it is not alarming.

CONCLUSIONS

For best results the drug must be given at the onset of the attack. If the patient is impressed with the fact that it must be taken as soon as he feels a headache is starting, this can be accomplished. Another factor of great importance is proper dosage. Two tablets seem to be required in the average case, and some patients may even require a third tablet shortly after the initial dose of two.

Other products containing the combination of ergotamine tartrate and caffeine have for a great many years enjoyed the reputation of being able to abort migraine headache. However, many of these products either do nothing for the gastrointestinal symptoms of migraine, or increase the nausea and vomiting, and add abdominal cramps. This preparation on the other hand, definitely relieved the nausea and vomiting of the attacks and in only 1.66 per cent of the cases did it produce any gastrointestinal side effects.◀

Cardiac Shock Treated by Metaraminol

An 80% mortality reported in shock following acute cardiac infarction is probably an underestimate since it is based on hospital experience alone. In a series of cases treated for shock by noradrenaline infusions within 3 hours of onset, only 13% died. Although noradrenaline infusion may be successfully carried out in the hospital, its employment in the home presents many difficulties and is therefore seldom used there. In 12 cases where shock was too severe to allow removal to a hospital, the immediate use of metaraminol by intermittent injection resulted in a mortality rate of 50%. All the patients with shock of 4 or more hours' duration died, demonstrating the need for early treatment of this condition.

Besterman, E. M. M., *Brit. M.J.*, 1:1081-1083,1959.

ORIGINAL ARTICLE

Experience with the Steroids in the Treatment of Bronchial Asthma

In asthmatic patients, a small maintenance dose of steroids builds up to normal level a deficiency of pituitary and adrenocorticotropin function

LESLIE N. GAY, M.D., *Baltimore, Maryland*

The author's interest in the treatment of bronchial asthma and asthmatic bronchitis began 30 years ago, when he was appointed the director of the Allergy Clinic of The Johns Hopkins Hospital. His experience over these many years with the many therapeutic approaches directed to the relief of the distressing symptoms associated with bronchospasm and obstruction makes possible an appraisal of the failures and successes of these remedies.

The work of Kendall and Hench has completely changed the methods of treatment of the asthmatic patient. The development of the steroids—adrenocorticotropin, cortisone, hydrocortone and prednisone—is comparable in therapeutic value to the asthmatic patient to that of insulin to the diabetic patient or to that of vitamin B_{12} to the patient with pernicious anemia. This opinion is based on experience with more than 300 patients who have suffered respiratory distress for from one to 50 years. Report is made on the etiology, the duration and the severity of symptoms in these patients, many of them having been under their care for more than 10 years. In their experience, no drugs or combinations of treatment have given these patients, irrespec-

DIFFERENTIATION OF ASTHMATIC PATIENTS

	Extrinsic	Intrinsic
Family History	Present	Usually absent
Sensitizing antibodies	Present	Absent
Age at onset	Early years	Middle age
Bronchial mucus	Present	Excessive
Complications	Pulmonary emphysema	Bronchitis, emphysema, cor pulmonale, periarteritis.
Specific treatment	Available	Symptomatic
Prognosis	Good	Uncertain
Mortality	Unusual	Over 5%

tive of age, duration of symptoms or etiology, the long remissions which have followed the treatment with corticotropin (highly purified in gelatin) combined with either hydrocortone or prednisone. Careful study of the patients before treatment has been the explanation of infrequent serious side reactions from these drugs.

The remarkable ability of the steroids (corticotropin, ACTH) and prednisone) to reverse the signs and symptoms of allergic and hypersensitive states has made them the most useful of all forms of therapy, and they have outmoded some of the older therapeutic agents.

STEROID TREATMENT

Many of the patients who suffered from intractable bronchial asthma and chronic asthmatic bronchitis were especially uncomfortable during the pollen season; others were affected by some environmental contact. All previous treatment had failed to give any of them more than transient relief. Discovery of the beneficial action of the steroids in the treatment of asthma has completely altered the outlook of the patients in this report, and the outlook for patients suffering from bronchospasm, irrespective of environmental or bacterial allergy, should be most optimistic.

A problem which confronts the physician in this country is the limited hospital space available for the chronically ill patient, to say nothing of the cost of hospitalization to the individual and to the state. The asthmatic patient, who falls in the category of "chronically ill," unfortunately has attacks of dyspnea so severe that he is completely incapacitated, often for many days. Paradoxically, he then becomes an acutely ill patient.

The author's experience with steroid therapy began in 1950, and his first report on its use in 75 cases, all ambulatory patients, was published in 1954. These patients were divided into four age groups: 3 years to 20 years; 20 years to 40 years; 40 years to 60 years; and 60 years to 80 years.

It is important to realize that, just as diabetes and primary anemia are not "cured" by specific agents, so bronchial asthma is not "cured" by steroid therapy. If the patient is negligent, relapse occurs in any one of these chronic diseases. The patients under treatment have been divided into two groups—the extrinsic group and the intrinsic group. Differentiation of the two is important, but irrespective of group, the results of treatment are comparable.

DISCUSSION

The first group of 60 patients who began treatment in 1950 has been recently reviewed. Three of the 60-80 age group have died from coronary artery disease, one from pneumonia which followed osteoporosis and multiple fractures. Two patients of the same group have had severe gastro-intestinal hemorrhages, but subsequently elected to again begin prednisone therapy rather than suffer from severe relapsing asthma. Relapses in all groups have occurred repeatedly, but in each instance a temporary increase in dosage of prednisone or a supplementary dose of ACTH gel gave rapid relief. A striking observation is that no relapse has been as severe or as prolonged as the attacks occurring prior to steroid therapy. Fortunately, the disease does not become resistant to the hormone after prolonged administration. In spite of numerous complications in the older groups of patients, *i.e.*, hypertension, diabetes, coronary artery disease, chronic sinusitis and marked emphysema, treatment has been continued, with cautious, repeated observation of the patient. The severity of the asthma has warranted the risk.

THE SECOND GROUP

Subsequently, more than 150 patients suffering from persistent bronchial asthma and asthmatic bronchitis have been studied and treated in precisely the same manner. They have been separated into similar age groups. Of those in the youngest group—6 to 20 years—only one patient had frequent relapses, though 10 reported a rare attack of asthma. Symptoms were completely controlled by 2.5 mg. to 10 mg. of prednisone daily. None of the group had any side reactions. Of the second age group—20 to 40 years—6 patients have had no relapses, 12 rarely have had relapses, and 14 have had frequent attacks of asthma. The average dose of prednisone for the group was from 5 to 15 mg. daily. Four patients discontinued treatment because of mental depression and gastro-intestinal discomfort. Of the third group of patients—40 to 60 years—11 reported no recurrence of symptoms after three years of treatment. Twenty patients rarely had a relapse, 12 reported frequent relapses. The maintenance dose of prednisone averaged from 5 mg. to 20 mg. daily. Three patients discontinued treatment because of gastro-intestinal discomfort.

OLDEST GROUP OF MOST INTEREST

By far the most instructive group is the oldest group of patients 60-80 years of age. The majority of these had severe asthmatic bronchitis and emphysema with marked shortness of breath. Five have had no return of asthma since they received their first steroid therapy. Twelve patients have had rare attacks and 9 reported frequent attacks.

It is the author's opinion that the continued use of steroids in the treatment of chronic bronchial asthma will reduce the number of patients who otherwise would attain old age in a state of chronic invalidism. Unlike the patient afflicted with rheumatoid arthritis, a disease which requires large doses of these drugs, for the asthmatic patient a small maintenance dose builds up to normal level a deficiency of pituitary and adrenocorticotropin function. So long as the physician is constantly on the alert for the unpleasant side-re-

actions which occasionally accompany steroid therapy, the treatment as outlined in this paper promises greater comfort to the patient than any other known therapeutic procedure.◀

Serum Sickness: Pathogenesis

A study of 133 diphtheria patients, 80 per cent of whom showed clinical manifestations of serum sickness and two-thirds of whom were children aged three to 15, pointed out the following forms of serum sickness:

1. An autonomic nervous form, characterized by increase in nervous tone without appreciable reaction in mesenchyma, blood, or lymph. This form runs a tedious course and is more common in moderately severe cases and in the 10 to 15 age group.

2. A mesenchymal form, in which the number of lympho-histiocytic elements in the fluid of cantharides blister show a rise. This form is common in mild cases of short duration and young children.

3. A serologic form, characterized by pronounced reaction in blood without other manifestations, and seen only when the condition is latent.

4. An anergic form, in which only mild clinical symptoms but no other changes are seen. This form is most common in young children.

These different manifestations may be related to differences in the reactivity of the autonomic nervous system and the mesenchyma at different ages.

Korowajew, E. N., *Allergie u. Asthma*, 5:1,1959.

ORIGINAL ARTICLE

Triacetyloleandomycin* in the Treatment of Acne Vulgaris

Triacetyloleandomycin therapy, either alone or combined with other measures, produced excellent results in 93 of 130 patients

M. MURRAY NIERMAN, M.D., *Calumet City, Illinois*

The use of antibiotics in the treatment of acne has been both praised and condemned, but the occurrence of local infection as one aspect of this disease has seemed to mark as reasonable this approach to therapy. The local use of such medication has been generally ineffective, and considered to be a source of sensitization to the drug being used.[1] Intramuscular penicillin has been reported to be useless, but the broad-spectrum antibiotics appear to be of value[1-3] and considered useful, especially when combined with estrogen therapy.[4] It has been reported that broad-spectrum antibiotics, in combination with local therapy only, are of value and of local action rather than the result of any alteration of the gastrointestinal flora.[5] Considerable benefits from tetracycline have been reported.[5]

We felt it worthwhile to try one of the newer antibiotic agents, triacetyloleandomycin, a derivative of oleandomycin.

Oleandomycin, a product of Strep-

*Tao®, J. B. Roerig & Co., Division of Chas. Pfizer & Co., New York.

1. Robinson, H. M., Jr., *A.M.A. Arch. Dermat.*, 69:414,1954.
2. Andrews, C. C., et al., 146:1107,1951.
3. King, W. C., & Forbes, M. A., *South. M.J.*, 49: 875,1956.
4. Becker, F. T., *A.M.A. Arch. Dermat.*, 67:173, 1953.
5. Stritzler, C., & Frank, L., *Antibiotic Med. & Clin. Therapy*, 5:109,1958.

tomyces antibioticus, was first reported on in 1954.[6] It has a spectrum of activity similar to erythromycin—the gram-positive organisms (including many penicillin-resistant staphylococci) and a few gram-negative organisms (Neisseria, Hemophilus, and Brucella)—and clinically has been found of value in the treatment of pneumonia, cellulitis, pharyngitis, surgical and traumatic wound infections, abscesses, gonorrhea and urinary-tract infections caused by susceptible organisms. Triacetyloleandomycin, the derivative compound, following ingestion in man is de-acetylated into at least six biologically active esters. All of these derivatives remain active throughout their presence in the body against gram-positive pathogens, including resistant strains of Staph. aureus.[7,8]

METHODS AND MATERIALS

One hundred and thirty-nine patients were treated (53 males, 86 females), ranging in age from six to 51, the largest number (85) being in the second decade. The vast majority (122) had pustular acne (many of them with cystic lesions, and five with rosacea). There were nine patients with acne of other varieties (keloidal, neurotica and conglobata), and eight instances of other pustular lesions (furunculosis or folliculitis).

Antibiotic therapy consisted of triacetyloleandomycin phosphate capsules, initially in a dose of 250 mg. four times a day for two days to two weeks; 100 of the patients for one week. Maintenance dosage thereafter was 250 mg. in 124 cases; 500 mg. was the daily regimen in 12 patients. The duration of maintenance therapy was for one week to six months. The drug was stopped because of urticaria in one patient, discontinued by another patient for no apparent reason; a third case required large maintenance doses. Other therapy included dermabrasion (37), Vleminck's solution (44), estrogens (40), x-ray therapy (19), vitamin A (9), ultra-violet radiation (6), thyroid (2), vitamin C (1), and steroids (1). Some cases had more than one additional mode of therapy. Eleven of the cases had no additional therapy, mostly those with non-acneiform lesions other than pustules.

One hundred and thirty cases were followed two weeks to six months after discontinuance of the antibiotic, the majority of them three months. Follow-up was by mail or otherwise inadequate in nine cases. The results were classified first at the end of antibiotic therapy as cured, controlled, or no improvement, and the duration of time for control or cure to be attained was noted. Next the occurrence of relapse after cessation of antibiotics was recorded, and finally the lesions were recorded as showing partial or complete involution and the total follow-up results as excellent, good or poor.

RESULTS AND DISCUSSION

In general the results of therapy were excellent in 93 cases of the 130 adequately followed, including five out of six of the acne rosacea type. Eighty-four of these cases had complete involution of the lesions. Twelve cases showed no improvement, and in two others the results were poor. Twenty-three cases had good results with only partial involution of the lesions.

The 23 cases that had therapy for a

6. Sobin, B. A., et al., A New Antibiotic, Antibiotics Annual, 1954-55, p. 827.
7. English, A. R., et al., *Proc. Soc. Exp. Biol.*, 100: 880,1959.
8. Celmer, W. D., et al., Paper read before Medical Chemistry, 133rd Meeting of the *American Chemical Society*, San Francisco, Calif., April 16, 1958.

hen holiday dinners include food allergens

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NTIHISTAMINIC-ANTISPASMODIC

ires prompt, comprehensive relief

The patient allergic to certain foods may find holiday menus a temptation difficult to resist. When he yields to allergenic dishes, BENADRYL brings him prompt relief from gastrointestinal distress. BENADRYL

schelps control cutaneous reactions and respiratory symptoms so often associated with od sens vity. BENADRYL Hydrochloride (diphenhydramine hydrochloride, Parke-Davis) availab in a variety of forms, including Kapseals,® 50 mg. each; Kapseals, 50 mg., with thelrine lfate, 25 mg.; Capsules, 25 mg. each; Elixir, 10 mg. per 4 cc.; and for delayed tion, E. lets,® 50 mg. each. For parenteral therapy, BENADRYL Hydrochloride Steriials,® 10 g. per cc.; and Ampoules, 50 mg. per cc.

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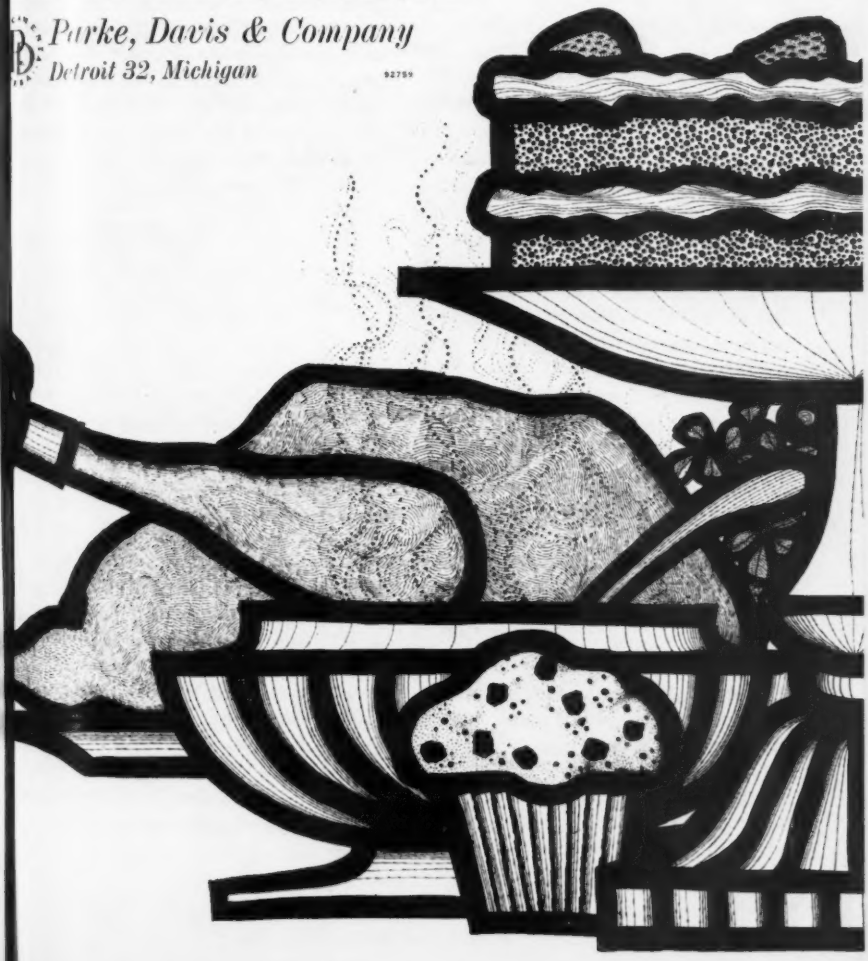


month or less had only five relapses, all occurring within one to two weeks of stopping the drug. All but one had prompt return to the pre-relapse condition upon further use of the antibiotic. Among the 40 treated for one to two months there were 10 relapses, at intervals of two weeks to three months, six of these responding well to further therapy. In the group of 42 cases treated for two to three months, there were twelve relapses, at intervals of two weeks to two months, five responding well to resumption of triacetyloleandomycin, and one responding better to tetracycline. Among the 13 treated longer than four months, eight had relapses, seven responding to subsequent employment of the drug.

It is important to note that most of these relapses (4 out of 5 treated less than a month, 8 out of 10 treated one to two months, 9 out of 12 treated two to three months, and all of those treated more than three months), occurred in the group controlled on triacetyloleandomycin therapy rather than cured. In other words, of 118 showing some improvement, 40 could not be considered cured, and in this group 29 relapses occurred. One therefore must consider the possibility that the improvement and relapse seen in these cases was coincidental with therapy, rather than the result of the exhibition and withdrawal of therapy, and the natural remissions and exacerbations characteristic of acne.

Since duration of therapy was determined by the individual patient response, no conclusions can be drawn as to the most desirable duration of therapy, either from the standpoint of the most cures to be obtained or the fewest relapses to be expected. Longer periods of therapy simply indicated that the patients had more difficult cases of acne, and hence would be expected to relapse more readily.

Of the 84 cases with complete involution of the lesions, 31 had a combination of dermabrasion and triacetyloleandomycin therapy (13 of these also combined with x-ray, estrogens, or Vleminck's solution). It was our impression that the treatment of pustular acne with scarring, first by dermabrasion followed later by triacetyloleandomycin, is an excellent approach to this problem. The dermabrasion is performed in the presence of the acute pustular reaction and the triacetyloleandomycin therapy instituted immediately following. The reason for the excellent response may be that dermabrasion makes the pustular cysts amenable to antibiotic therapy.

Of the 14 poor results, one responded best to penicillin and dermabrasion, two to tetracycline, two to oxytetracycline, one to sulfonamides, and one to x-ray therapy. One failed to respond to any antibiotic, and in two cases no other antibiotic was tried. One patient had a relapse and did not report for follow-up therapy, and one was uncooperative and irregular in her use of therapy. Two patients worked with industrial oils or irritants which exposure seemed to be a major factor in the causation of their acne.

The eight cases of chronic folliculitis or furunculosis were all considered cured, with complete involution of the lesions, all of them except one (who had vitamin A) without other therapy than triacetyloleandomycin. Five of these patients had a history of furunculosis dating back one to five years.

Eleven patients had no therapy except triacetyloleandomycin; seven of these were in the furunculosis group just discussed, while only four had acne. Three of these four had an excellent result and were considered cured with complete involution of the lesions. One who had had previous dermabrasion showed only a partial clearing of his lesions and had a relapse after stopping the antibiotic. The group of acne patients treated with triacetyloleandomycin alone is too small to permit evaluation of this agent by itself in the therapy of acne. In combination with the other measures used, however, particularly dermabrasion, it appeared to be of great value.

SUMMARY

One hundred and thirty-one cases of acne vulgaris and eight cases of chronic furunculosis were given a new antibiotic, triacetyloleandomycin, for periods of one week to six months, along with other recognized forms of therapy.

Adequate follow-up data were available, after stopping the drug, on 130 patients.

The results were excellent in 93, good in 23, and poor in 2. In 12 patients there was no improvement.

Relapses were observed in 35 cases, 29 of these in 40 patients who showed control rather than cure initially. Though 22 of these 35 relapses (4 of the 6 cases initially cured) appeared to have prompt remission with further use of triacetyloleandomycin, one must consider the possibility that these were natural remissions and exacerbations of acne, rather than any drug effect, in the group not cured initially.

The impression was formed that the combination of dermabrasion and triacetyloleandomycin was suitable for the complete treatment of acne.

Excellent results were obtained with triacetyloleandomycin alone in a small number of cases of furunculosis. If combined with a low-carbohydrate diet, triacetyloleandomycin given over a prolonged period may well be the agent of choice in the treatment of furunculosis.◀

Nephrotic Syndrome: Pathogenesis

The permeability of the glomerular capillaries is increased in nephrotic syndrome, resulting in excretion of proteins normally retained. Consequently hypoproteinemia associated with a fall in osmotic pressure and the formation of edema develops. Albumin excretion alone, however, cannot fully account for the early appearance and the extent of hypoproteinemia. Although impaired protein synthesis had been suspected, it was shown to be normal or even increased. The hypothesis that nephrotic syndrome is accompanied by hypothyroidism has also been disproved.

It is more likely that the edema is caused by a combined effect of the following factors: reduction in osmotic pressure; increase in anti-diuretic substances (since the posterior pituitary is stimulated as a result of the diminution in the amount of circulating blood); increase in the sodium-retaining adrenocortical hormones; and secondary hyperaldosteronism. Hypoproteinemia appears to disrupt potassium metabolism. Hyperlipemia may result from fat mobilization following hypoproteinemia and malnutrition.

Quirno, N., *Rev. Asoc. méd. argent.*, 72:213,1958.

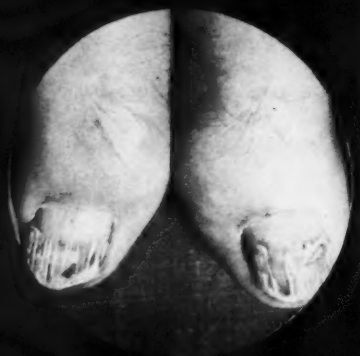
BREAKTHROUGH IN THE TREATMENT OF RINGWORM INFECTIONS

GRiFULVIN

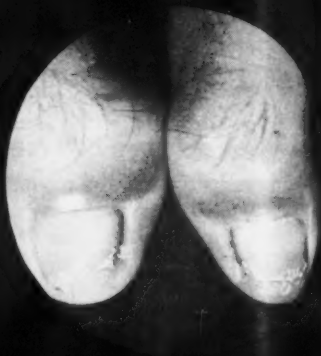
Griseofulvin

ORALLY EFFECTIVE IN FUNGOUS INFECTIONS OF SKIN, HAIR, AND NAILS[1-4]

DRAMATIC IMPROVEMENT IN TRADITIONALLY REFRACTORY RINGWORM INFECTIONS



Tinea of the hand, 7 years' duration—after 4 months of treatment with Grifulvin. Infecting organism, **Trichophyton rubrum.**



Same patient after 6 months of treatment with Grifulvin. Infection has cleared; healthy nail growth is almost complete.

McNEIL

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ORIGINAL ARTICLE

"Let's Order Some X-rays"

Close rapport between the general practitioner and the radiologist is required when any roentgenologic study is done

HERBERT R. ZATZKIN, M.D.,* *Hempstead, New York*

How many of our fellow practitioners, when faced with a perplexing battery of complaints are apt to try first a short cut to diagnosis and say, "Let's order some x-rays." It is not to deny the very important role that properly exposed roentgenograms may play in arriving at a diagnosis, but rather to caution lest this casual and off-hand suggestion result in equally casual and often needless exposure to x-rays.

RESPONSIBILITY

In this day of public awareness and overconcern with possible deleterious effects of ionizing radiations, the entire medical profession must share the burden of insuring that x-rays are properly utilized. While the radiologist should employ all his talents to obtain radiographs of excellent photographic and anatomic likeness in a fashion insuring full patient safety, he may unwittingly contribute to needless patient exposure if he goes along with a request that he expose to x-rays a patient whose condition may be much better diagnosed by methods incapable of doing harm.

The medical and lay press have dramatized the dangers of x-rays to a degree where further warnings and suggestions are not apt to be heeded. The time has come to tackle a problem much more fundamental in our still ever present challenge to reduce

*Director of Radiology, Meadowbrook Hospital, Hempstead, N.Y.

x-ray exposure, and the problem rests upon the doorstep of the general practitioner.

I refer to the manner in which roentgenograms and fluoroscopy are ordered, or performed, by the general practitioner of medicine. If the radiologist is utilized as a laboratory technician and exposes x-rays ordered without prior consultation, in many instances the patient has either an incomplete study, or one poorly designed to assist the practitioner in the management of the case.

As a radiologist performing services for many general practitioners, perhaps a few instances encountered in private as well as hospital practice will illustrate this point.

THE PATIENT WITH A "HEADACHE"

A patient recently presented himself with a note from his physician which stated "Headaches. Please take Skull X-rays." Five minutes of interview elicited the information that this patient's headaches dated from his change of occupation requiring that he move from the Midwest to the South Shore of Long Island. His headaches were frontal and worse when he was recumbent and he did much hawking and spitting of phlegm. With this history, I took x-rays of the skull and included a Waters projection to show his paranasal sinuses. This man's trouble was related to a severe frontal sinusitis.

Another patient's introduction for x-rays was scribbled on a prescription slip which stated, "Rule out Temporal Arteritis or Brain Tumor. Take X-rays of Skull." A few minutes of questioning elicited the information that his pains had come on after the extraction of some posterior molars several months previously. In addition to the skull x-rays, I took open- and closed-mouth views of his temporomandibular joints, and readily demonstrated the difficulty resulting from a change in this man's "bite" secondary to his dental extractions.

THE PATIENT WITH NECK AND BACK PAIN

Of equal frequency are persons whose referral slips simply state "Take x-rays of neck for cervical rib," occasionally with "Patient has tingling sensations in arms" or "shoulder pain."

To the radiologist, x-rays of the neck usually imply soft-tissue technique such as is utilized to look for a foreign body. What is really desired, however, is an x-ray of the cervical spine. The routine exposure of a cervical spine consists of a single AP and lateral view, and some radiologists include an open-mouth projection to show the odontoid. The most important views are often neglected —simply because they are not asked for. The cervical spine should never be x-rayed unless views are taken in flexion and hyperextension as well as right and left oblique projections. An apparently normal neck, as seen in a single lateral view, may be incapable of flexing and extending through a normal range of motion and signify muscle spasm, the cause of which may then be ascertained. It is in the oblique view that the intervertebral foramina are seen, and here destructive processes may be readily detected.

To the practitioner who orders "Views of the Sacroiliac Joints," I would say that the incidence of true roentgenographically demonstrable pathology in these joints is extremely low. Symptoms referable to this re-

ion are more often due to disorders affecting the lumbosacral spine. Study of the lower spine with a view of the pelvis will give all the information needed concerning possible pathology in the sacroiliac joints. Oblique views at L5-S1 to show facets similarly will project the sacroiliac joints "en face" and serve a double purpose.

THE PATIENT WITH ABDOMINAL PAIN

The ordering of x-rays of the stomach, colon and gallbladder is often much abused. By making these studies in improper sequence patients are subjected to needless inconvience and ofttimes their difficulties go undetected. Many is the time I have been requested to give a patient "a swallow of barium" to see why he has dysphagia, in lieu of a complete gastrointestinal series. In so doing, I risk errors of omission concerning possible gastric pathology which may underlie the patient's difficulty.

There is also a tendency to say, "We'll examine the entire tract from esophagus to rectum for a midepigastric mass, so let's start with a barium enema." In heavens' name, why waste the time, subject all concerned to needless ionizing radiations and fill the bowel with barium so that the all important gastrointestinal study is rendered less than ideal when done? Let us demonstrate the most likely site of pathology first and not beat around the bush with accessory studies.

THE PEDIATRIC PATIENT

The problem is of considerable significance when x-ray studies are to be ordered for children. The potential danger to the gonads is lessened by careful gonadal shielding and one should insure that the radiologist performing this service is properly oriented in this regard. It is axiomatic that certain ailments, if allowed to progress undetected, can do infinitely greater harm to the patient than any possible genetic or hematopoietic damage from diagnostic exposure to roentgen rays. So far as we know, there is no documented case of any adult or child being damaged in any way by the diagnostic use of roentgen rays. This is, of course, excludes fluoroscopy, and here again a word of caution must be added. The routine use of the fluoroscope in the physical examination of children cannot be too strongly condemned. This valuable procedure should be reserved for the study of motion (of the heart, of the diaphragm or mediastinum) when sound indication exists. And it must be kept in mind that though the fluoroscope generates not more than 5 *r* per minute, gonadal shielding is in order.

THE PATIENT WHO COMES WITH X-RAYS

With all due apologies to the physician who practices within the limits of his capabilities, attention should be called to a very prevalent practice which gives our entire medical profession a bad name. I refer to the patient coming to the radiologist for an x-ray examination, bringing along x-ray pictures made by his general practitioner. In my experience in no more than 10% of such instances has the patient received an adequate examination. In most cases the films are either black or blank, and often look as if someone had eaten his lunch on them. I have seen alleged gastrointestinal series which consisted of three to four hazy views of a barium filled stomach, obviously exposed with a non-rotating anode tube, and always without accompanying spot films. This

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is a wicked and dangerous situation which we in the profession must correct.

Of course, any possessor of an M.D. degree may perform whatever medical acts the statutes of his State sanction, the regulations of his hospitals permit, and the dictates of his conscience allow. Untrained in abdominal surgery, in electrocardiagraphy, in cystoscopy or cardiac catheterization, most physicians relegate such procedures to those who have had additional training and exclusively perform such studies. Such self discipline by no means always obtains when it comes to radiology. Considering the years of training required for accurate film interpretation, or the making of a gastrointestinal x-ray study, it is nothing short of amazing that so many of our young physicians, fresh out of their internships, purchase x-ray equipment and undertake the most difficult of roentgen diagnoses. One can only suppose that they have not been impressed with the proper role of radiologic investigation during their training periods.

It is inconceivable that any physician charged with a patient's welfare, his very life, would content himself with such obviously inadequate studies. With my faith in our profession, I wholeheartedly reject any other motivations, and ascribe such conduct entirely to a deficiency in the education of some of our colleagues. One who knows what is requisite for the proper performance of a gastrointestinal series will never countenance sub-standard studies.

WHAT CAN BE DONE?

It is easy to offer criticism but hard to make practical suggestions for the correction of loose or dangerous practices. I offer several thoughts which may be helpful.

Before requesting or performing x-ray studies, ask:

1. Is this study designed to show the pathologic state I suspect?
2. Would some additional views increase my chances of discovering what is wrong with my patient?
3. Is my equipment "safe" and can I expose roentgenograms so as to deliver no or very little dosage to the patient's gonads?
4. Is the radiologist who is to make these studies for me fully aware of minimal dosage techniques, and does he shield patients' gonads?
5. Have I given the radiologist sufficient history so that he and I can hold a real consultation?
6. Could x-ray studies of any of my patients in the first trimester of pregnancy be just as well deferred till a later date?
7. Am I denying a patient an x-ray examination because he has already had too much x-ray? If so, do I know this to be a fact, or am I succumbing to popular misinformation and hysteria?
8. Have I analyzed the urine before ordering an excretory pyelogram?
9. Have I done a rectal examination before ordering a barium enema?
10. And perhaps most important of all, "Is this examination really necessary?"

From the foregoing, it is obvious that close rapport between the general practitioner and the radiologist will help to arrive at a solution to these problems. The aim should be to do the correct examination the first time and do it well. The advances in all medical fields have been such that no one man can

be master of them all. The radiologist has all he can do to keep abreast of developments in his field and it cannot be expected that those who expose an occasional radiograph will be equally equipped to obtain a good film and to be able to interpret all it may have to offer.

Unless we in the medical profession check the growing tendency to use x-rays indiscriminately, unless we offer the best in roentgen interpretation, and unless we insure that best proper protection be afforded in every case when x-rays are used, the public will demand that such steps be taken. There is a growing public sophistication concerning the quality of medical care offered in the United States today. Unless we give this matter serious thought, I do fear that other agencies will be able to step in and gain a foothold that may ultimately destroy the sound patient-doctor relationship we all cherish in this country today.◀

Essential Hypertension: Early Treatment

Some evidence supports the opinion that persistent elevation of arterial pressure is a leading, if not the primary, cause of organic cardiovascular damage in hypertensive patients. Although watchful waiting seems justified in the labile, middle-aged, usually female, hypertensive patient, it may not be justified in other patients with blood pressure no higher but more continuously elevated. Organic arteriolar changes usually are years in developing, and are possibly caused by arteriolar spasm.

The patient with hypertension is more likely to have atherosclerosis than are others. The incidence of myocardial infarction is four to five times greater in hypertensive men than in the general population, and 20 times greater in hypertensive than in normotensive women. The incidence of cerebrovascular atherosclerosis and thrombosis is increased among hypertensive patients, the atherosclerosis being a possible result of the elevated pressure or of an unknown but related circulating toxic factor. Atherosclerosis is limited in each case to areas of elevated pressure, indicating that this is the result of hypertension.

Conservative treatment of the young patient with benign essential hypertension is valid only if such a patient can anticipate a normal, or nearly normal, life span. A survey of cases of hypertension first recognized while patients were in their 30's showed time from onset to death in untreated patients averaged 20 years. Follow-up data on hundreds of thousands of insured persons showed the higher the pressure the shorter the life span. Although the prognosis for middle-aged women with extremely labile blood pressure seems good, they should be differentiated from male hypertensives and from all young patients with persistent elevation of diastolic pressure.

There is evidence that prolonged elevation of blood pressure causes organic damage. Although the practice has been to reserve antihypertensive therapy for patients with organic complications, it should be seriously considered for patients under 45 if hypertension persists under basal conditions or is progressive.

Freis, E. D., *Heart Bull.*, 8:52-54,1959.

CASE REPORT

Systemic Scleroderma: Survival of a Patient for Twenty Years

In each of four hospital admissions the course of the disease was reversed, primarily by adrenocortical therapy and high-salt intake

JOSEPH JOEL FRIEDMAN, M.D., *Unadilla, New York*

A married dairy farmer of 51 was admitted to a hospital with "arthritis" or "rheumatism" in his hands and feet for 12 months, indigestion and burning sensation in the stomach for eight months and anorexia for two months. He had lost 30 pounds. After silo-filling time in the fall his fingers had begun to swell and feel stiff, the skin on his fingers and soon afterward that on his feet becoming warm, red, and stiff. The stiffness of hands and feet became more painful and crippling. He grew pale and weak and was admitted to the hospital.

The patient was alert and cooperative, in no distress, and neither cyanotic nor jaundiced. Temperature was 99.8°, respirations 20, pulse 80 and blood pressure 112/70. Skin was well tanned and firmly pigmented about neck and forearms. There were no eruptions. Abnormal findings were a red, mottled, warm, moist, firm, seemingly thickened skin, and slightly limited motion. Admission diagnosis was rheumatoid arthritis, vascular disorder and a protein deficiency due to faulty diet—all questionable.

For the past six weeks he had experienced stiffening of the face, jaws and abdominal muscles. The clinical diagnosis of scleroderma was made

on the thickening of the skin, the brawny edema of the hands and feet, acrocyanosis, and the stiffness of the muscles of the hands and feet. He was discharged after nine days in the hospital.

Signs and symptoms were progressive for the next two years after which time collapse suggestive of adrenal failure was treated with 10 cc. of adrenal cortical extract, one injection intramuscularly, and with saline solution orally and intravenously. Recovery was remarkable. On continued small doses of adrenal cortical extract and on a high-salt, high-protein, high-fat diet, he gained 12 pounds, felt stronger, became ambulatory, and seemed to be in remission. The adrenal cortex extract was discontinued after several months.

Five years later he was readmitted to the hospital for extreme weakness, cough, nausea and vomiting. Weight was 125 pounds, blood pressure 90/60. He was treated with adrenal cortical extract 1 cc. every two hours, ephedrine sulfate 3/8 gr. every four hours, and hypertonic saline solution intravenously and orally. His condition was good when he left the hospital four days later.

After another period of five years, he was again admitted with nausea, vomiting, exhaustion, and loss of weight of 13 weeks' duration. He weighed 90 pounds at this time and the skin all over his body was tight and hard. Complaint was made of pains in body and chest muscles, and the patient presented fixed flexion of fingers, slight stiffening of the spine, and very stiff ankles. Movement at shoulders, elbows, wrists, hips, and knees were very limited. He was treated for four days with saline intravenously, and adrenal cortical extract, testosterone, vitamin B_{12}, and B complex parenterally in large doses. Soon he was back on a high-carbohydrate, high-protein, and high-salt diet, after which he recovered quickly and felt quite well for the next four years. At the end of this time his disability increased due to stiffness. He became bedridden and was readmitted to the hospital for seven days with marked weakness, difficulty in swallowing, crippling of extremities, pallor, and a small bed sore. His weight was 95 pounds, blood pressure 170/80. He had a marked sclerodactyla with complete contracture deformity of both hands. The ECG revealed myocardial degeneration, sedimentation rate was 38 mm., hemoglobin 7.8 gm.%, while cells 5,750—60% segmented forms and 3% eosinophils —cholesterol 159 mg.%, chlorides 670 mg.% and urea nitrogen 143 mg.%. X-ray films showed marked arthritis of the lumbar spine, pelvis and hip joints, and calcification of both the iliac and right renal arteries. Blood transfusions raised the hematocrit to 44, hemoglobin to 15 gm.%. Response to treatment was prompt and his condition continued to be good until three years later, when death ensued four days following admission. For many weeks before he had been eating less, losing weight, growing paler and thinner, and for one week he had been obstipated. A large fecalith was removed from his rectum, and his bowel was relieved with high colonic irrigations. He weighed 55 pounds at his last admission to the hospital and was too exhausted and weak to swallow or to move. All extremities were flexed and fixed. Pulse was 120, blood pressure 90/60.◀

New York J. Med., 59:2235-2238,1959.

Low Back Pain

Most patients respond successfully to bed rest, application of heat, analgesics, flexion exercises and controlled activity

VIRGIL R. MAY, JR., M.D., *Richmond, Virginia*

Generally there are two broad classes of low back pain:

1. Those which occur rapidly as the result of an injury or excessive stress and strain.

2. Those which are caused by faulty mechanics, congenital anomalies and progressive pathological conditions.

The most common cause of low back pain is probably simple sprain of the joints of the vertebrae, usually complained of in the early summer when too vigorous exercise is indulged in after months of relative inactivity. Many of these patients, continuing to overstrain after the initial attack has subsided, seek medical advice the following day when the pain and stiffness become disabling. In the interval between the time of the injury and the following day it is believed that the fascia, ligamentous structures and muscles contract and become edematous, thereby causing the disability. Bed rest, along with the administration of analgesics, application of heat in the form of heating pads, diathermy, and heat lamps, will usually cure the patient in a few days. When joint tenderness is present, infiltration with 1 per cent Novocain will relieve spasm and pain.

Compression fractures or fractures of the articulating pedicles may be caused by very slight injuries, especially in elderly persons. For this reason x-ray diagnosis is recom-

mended for all patients complaining of low back pain, regardless of how trivial the injury may seem.

Congenital anomalies in the low back area are not uncommon and usually benign. The most frequent site of low back pain may be in relation to a congenitally unstable lumbosacral articulation, permitting an undue amount of motion at the lumbosacral joints. Posterior displacement of the fifth lumbar vertebra on the sacrum is a frequent cause of excessive mobility. Other mechanical causes of low back pain include:

1. Vulnerability of the invertebral foramina by its alteration in size and shape through the mobility of the intervertebral discs and articular facets.
2. Laminae of the fifth lumbar or first sacral may not be united in the midline. When the defect is narrow and there is no protruding sac it is not significant except as a cause of additional weakness when other defects are present.
3. An acute lumbosacral angle.
4. Unilateral or bilateral sacralization of the fifth lumbar vertebra transverse processes.
5. Spondylolisthesis.
6. Posterior protrusion of the lumbar invertebral discs.

In the majority of patients treatment should be conservative, surgery being reserved only for those having recurrent attacks and failing to respond to conservative treatment. The plan of conservative treatment is aimed at relief of pain, relaxation of muscle spasm, regression of inflammation, correction of the deformity and returning the patient to useful activity. Acute severe cases are best treated with bed rest (the back and knee rests raised to about 45 degrees), heat, narcotics, and salicylates. As soon as feasible, flexion exercises are given to tone up the support muscles and to teach the patient to maintain his lower vertebrae in physiological balance. Instructions to the patient are:

1. Never sleep on your abdomen, but rather on your side with your knees drawn up.
2. Never bend backward or reach up overhead backward.
3. Never lift loads in front of you above waistline level.
4. Sit with the pelvis rotated in a slightly "slumped" position.
5. When possible, elevate the knees higher than the hips when sitting.
6. Avoid standing and wearing of high heels as much as possible.

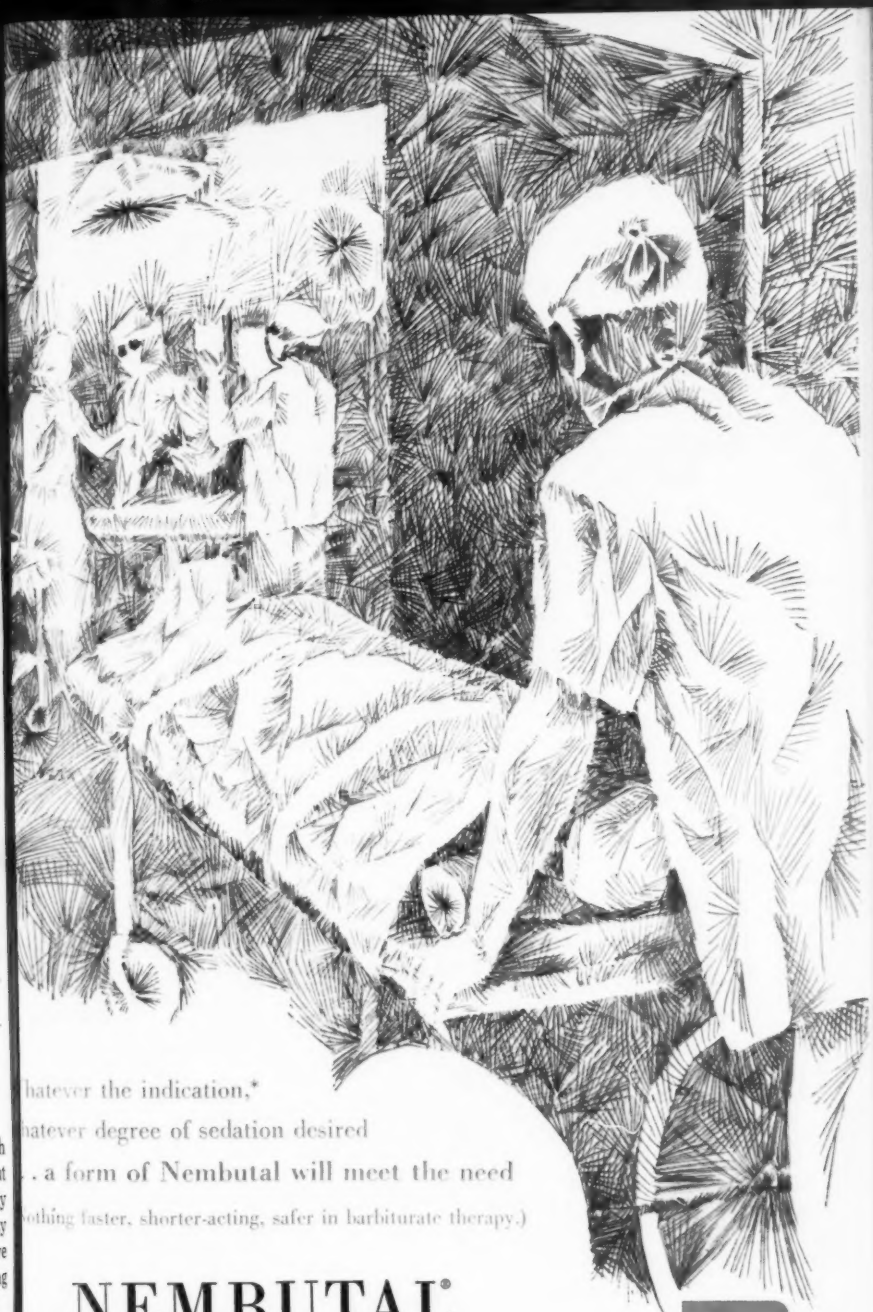
If flexion treatment fails, fusion of the spine in flexion should be performed to maintain the normal relationship of the lower lumbar vertebrae.◀

Virginia M. Month., 86:197-201,1959.

Taste Sensitivity: Effect of Aging

Taste thresholds for sucrose, sodium chloride, hydrochloric acid, and quinine sulfate determined in 100 subjects ranging in age from 15 to 89 years demonstrated that little change in taste sensitivity occurs until the late 50's, when it decreases appreciably in both men and women. Though loss of these 4 taste primaries is about equal, that of sourness is apparently least pronounced. Loss of sensitivity is presumably due to degenerative changes in the receptors. Smoking does not appear to be a factor.

Cooper, R. M., et al., *J. Gerontol.*, 14:56,1959.



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Surgical Treatment of Convergent Strabismus

Cases requiring operation should be treated as early as possible to allow the binocular reflexes to develop properly

FLOYD M. BOND, M.D., *San Diego, California*

Concomitant strabismus is a dissociation of the eyes wherein the deviation remains the same in all directions of gaze. It has been divided into two types:

1. Primary concomitant strabismus, due to the effect of an obstacle in the sensory (afferent) paths of the binocular reflexes or in their central organization, so that the eyes, visually dissociated but coordinated by the postural reflexes, retain their motor taxis unimpaired. The squint occurs during the development of the binocular reflexes, its essential feature being failure in binocular single vision.

2. Secondary concomitant squint, owing to abnormality (usually paresis) of a peripheral muscle. Commonly a weakened muscle on one side is opposed by a contracted muscle, the condition eventually bringing about permanent structural changes. For this reason the deviation, originally apparent only on movement of the action of the afferent muscle, later becomes evident in all directions of gaze, and persists after the paresis is cured.

CLINICAL TYPES

There are three clinical types—monocular, intermittent, and alternating. About 82 per cent of concomitant squints are monocular, the remainder being about equally divided between intermittent and alternating.

According to treatment they are classified as accomodative, partially accomodative and non-accomodative. Operation is almost always required for alternating strabismus and for whatever part of partially accomodative strabismus glasses are unable to correct. Cases requiring surgery should be treated early so that the binocular reflexes will have a chance to develop properly.

INDICATIONS FOR SURGERY

Factors to be considered when contemplating surgery are the age of the patient, age of onset, duration of squint, refraction, visual acuity, anisometropia, amblyopia, amount of deviation, intermittency and variability of the angle of deviation, secondary deviations, rotation, abduction and adduction, vertical component and near-point of convergence. Mechanical factors include size and attachments of ocular muscles, contractures, anomalies of check ligaments, irregularities of the size of globes and orbits, and visible lesions of the media, the fundus or the optic nerve. In older children, the status of retinal correspondence, suppression, fixation habits and fusion are further considerations.

For congenital convergent strabismus or convergent strabismus developing within the first year of life, operation should be conservative. A bilateral 4 mm. recession of the medius rectus muscle or a unilateral 4 mm. recession of a medial rectus along with a 7 or 8 mm. resection of a lateral rectus is a conservative and safe procedure in these cases. Frequently patients with this type of strabismus will require further operation.

If the onset of strabismus is between one and three, and if non-surgical treatment has failed, operation should be not delayed. If it occurs after age three, operation may be delayed for a considerable time, during which glasses and other non-surgical measures should be tried.

In most cases there is an excessive amount of adduction so that the medial rectus of one eye or both eyes should be recessed and a lateral rectus resected. The angle of deviation should be measured with each eye fixing, the operative aim being to correct the lesser angle. If an associated abnormal vertical alignment is slight, it may disappear following correction of esotropia or be controlled with prisms incorporated in the glasses. If it is of considerable degree it may require attention at the same time the esotropia is corrected.

THE MEDIAL RECTUS

The tendon is dissected free from Tenon's capsule and from the superficial conjunctiva, after which the check ligaments are freed. The tendon is cut free from the insertion close to the sclera with scissors. Two fixation forceps with locks are placed at each end of the original insertion for fixation and stabilization of the globe and the superficial scleral sutures of fine catgut placed at the desired distance back of the original insertion. If a clamp is used on the muscle, the sutures should be placed in mattress fashion in the very end of the muscle tendon distal to the clamp to preserve as much tendon as possible. The recession of a single medial rectus muscle is done only in patients with a convergence excess and a relatively small deviation.

THE LATERAL RECTUS

In convergent strabismus the later-

al rectus may be resected, cinched, or tucked. Usually 5 to 10 mm. of the tendon is excised in resection and 5 to 12 mm. in tucking. The tendon must be thoroughly cleaned of Tenon's capsule and of the sheath in tucking so that when it is folded upon itself the flat surfaces will grow together. The tendon is not cut, the amount involved in the operation being as varied as the amount excised in resection.

Because recessions are more effective immediately and more lasting than resections and tucks, and adduction is usually much greater than abduction in a normal patient, it is rational to include a recession in most patients with a convergent deviation. Frequently a resection on the lateral rectus must also be made at the same time to gain the necessary amount of correction. When the two operations are combined, there is a greater and more immediate effect.

The choice between recession and resection depends on the individual case. Care must be taken not to alter any one muscle so much that its normal physiological action is impaired. Versions and ductions must also be satisfactory after operation. Generally a 5 mm. recession of a medial rectus and an 8 to 10 mm. resection (or 10 to 12 mm. tuck) of a lateral rectus is adequate and reasonable as a maximum when functional cure is the goal.

OPERATIVE PLAN

A clue to the best operative plan can usually be obtained from the study of rotations. In a case of alternating convergent strabismus in which the angle of deviation is 15 diopters, a 5 mm. recession of the medial rectus or a 10 to 12 mm. tuck of a lateral rectus is made. In angles of 20 to 30 diopters, with or without accommodative element, a 3 mm. recession and a 6 to 8 mm. tuck is usually sufficient. Angles of 30 to 40 diopters are corrected by a 4 mm. recession and an 8 to 10 mm. tuck, or a symmetrical bimedial recession of 3 to 4 mm. In cases of 40 to 50 diopters of deviation, a 5 mm. recession and an 8 to 10 mm. tuck, or symmetrical bimedial recessions of 4 mm., are generally adequate. If the deviation is 50 diopters or more, a 5 mm. recession and an 11 to 12 mm. tuck is made.

Monocular esotropia with near-equal visual acuity and with an angle of deviation greater for near than for distance is treated as follows: Deviation of 15 to 20 diopters by receding the medial rectus 5 mm. or tucking the lateral rectus 8 to 12 mm.; of 20 to 30 diopters by receding the internus 3 mm. and tucking the externus 5 to 6 mm.; of 30 to 40 diopters by receding the internus 4 mm. and tucking the lateral rectus 6 to 8 mm.; of 40 to 50 diopters by receding the medial rectus 4 mm. and tucking the externus 10 to 12 mm.; and of 50 diopters or more by receding the medial rectus 5 mm. and tucking the lateral rectus 12 mm.

In monocular esotropia with amblyopia (20/30 to 20/70) with good fixation of the deviating eye and excess of adduction, if the angle is from 20 to 30 diopters, the medial rectus is receded 3 to 4 mm. and the lateral rectus is tucked 5 to 7 mm. If the angle is from 30 to 40 diopters the medial rectus is receded 4 mm. and the lateal rectus is tucked 8 to 10 mm.; if from 40 to 50 diopters the medial rectus is receded 4 mm. and the lateral rec-

tus is tucked 8 to 10 mm.; and if 50 diopters or more the medial rectus is receded 5 mm. and the lateral rectus is tucked 10 to 12 mm.

Residual deviation and esotropia can be corrected later by operation on the other eye.◀

California Med., 90:433-436,1959.

Hydrochlorothiazide: Mode of Action

The effect of hydrochlorothiazide was studied and compared with that of chlorothiazide in a number of normal test subjects placed on an electrolytically constant diet for several months. The daily dosage for hydrochlorothiazide ranged between 6.25 mg. and 200 mg. and for chlorothiazide between 250 and 2,000 mg. Administration of one drug was interrupted for about a week before starting the other.

Results showed some similarity of action between the two drugs but also quantitative and qualitative differences. When both were given in equal amounts by weight, sodium excretion in response to hydrochlorothiazide was 40 times greater, chloride and water excretion 50 times, potassium excretion 30 times, and bicarbonate excretion 3 times greater. Urinary pH was not appreciably affected by hydrochlorothiazide while with chlorothiazide there was an appreciable tendency for it to become alkaline. Chlorothiazide attained an optimal effect at a dosage of 1,000 mg., hydrochlorothiazide at that of 20-25 mg. Larger doses of hydrochlorothiazide provoked a further increase in fluid and electrolyte excretion. Although the onset of effect of both drugs was equally prompt, hydrochlorothiazide remained fully effective after the effect of chlorothiazide had fallen off considerably.

Bartorelli, C., et al., *Schweiz. med. Wschr.*, 89:331, 1959.

Nephrotic Syndrome: Relations to Serum Protein Level

To find an explanation for the effect of drugs on protein elimination in chronic renal diseases, albumin excretion was investigated following the administration of prednisolone and human albumin and following various combinations of these two substances in seven patients with nephrotic syndrome. In the patients receiving only prednisolone (40 mg. daily), albumin excretion diminished, while in those given albumin intravenously, it rose considerably but fell quickly again following the addition of prednisolone. In the patients receiving an injection of albumin following pre-treatment with prednisolone for 14 days, the rise in urinary protein excretion was much less pronounced.

Results of the investigations suggest that:

1. Prednisolone can reduce protein excretion for considerable periods in patients with nephrotic syndrome.

2. Human albumin alone provokes an increase in protein excretion.

3. Additional prednisolone can suppress the increase in protein excretion produced by administration of albumin.

From the foregoing it appears that treatment with human albumin following appropriate pre-medication with prednisolone is the best method of raising serum protein levels in nephrotic syndrome.

Lachnit, V., *Med. klin.*, 53:1688,1958.

Glaucoma and the General Practitioner

The general practitioner is often the first to discover glaucoma among his patients and should refer more difficult cases to an ophthalmologist

CLAY W. EVATT, M.D., *Charleston, South Carolina*

Glaucoma may be divided into primary and secondary, acute and chronic, and still further into subtypes. This is a discussion of the closed or narrow angle and the open or wide angle types.

GLAUCOMA COMMONLY SEEN BY THE GENERAL PRACTITIONER

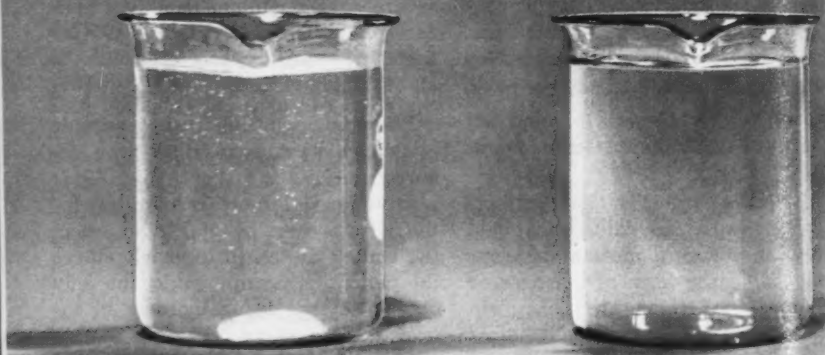
There is a large group of patients with narrow or partially obstructed angles in whom glaucoma develops gradually in the form of episodes or prodromal symptoms. They complain of cloudiness of vision, colored haloes around street lights, and tenderness and a feeling of pressure in the eyes. At first the episodes are of short duration, but may later develop into full-fledged attacks associated with severe congestion and pain. The general practitioner should refer all patients with this type of glaucoma to an ophthalmologist.

Wide angle or open angle simple glaucoma is a more insidious type, occurring mostly in patients over 40. It is considered largely responsible for the 300,000 cases of total blindness in the United States. In the early stages the patient is asymptomatic, the only diagnostic sign being increase in intraocular pressure. As the disease progresses, the pressure causes a cupping and pallor of the optic disk and pushes the vessels to the nasal side above and below the cup. When the

avoid the risk of insoluble, irritating aspirin particles

Chief among the drawbacks to aspirin usage is gastric intolerance. This ranges from mild upset and "heartburn" to severe hemorrhagic gastritis.[1-10] Studies performed in conjunction with gastrectomy[4, 5] and gastroscopy[2] have shown insoluble aspirin particles firmly adherent to the gastric mucosa and imbedded between rugae. Reactions varying from mild hyperemia to erosive gastritis have been reported to occur in the areas immediately surrounding these adherent particles.[2, 4, 5] This is reported to be particularly true in patients with peptic ulcer.[4]

CALURIN is the freely soluble, stable calcium aspirin complex. Its high solubility forestalls gastric irritation or damage



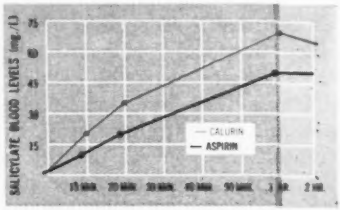
Regular aspirin crystals 24 hours after being mixed into water.

Calurin crystals in solution one minute after being mixed into water.

CALURIN*

STABLE SOLUBLE CALCIUM-ACETYLSALICYLATE-CARBAMIDE

Particle-induced ulceration — section through lesion found in gastrectomy specimen. An aspirin particle was found firmly imbedded in this undermined erosion. Such lesions may be associated with the relative insolubility of aspirin, which remains in particulate form after dispersion in gastric contents.



Calurin, being freely soluble, is promptly available for absorption into the systemic circulation. Salicylate blood levels in 12 subjects receiving both Calurin and plain aspirin were found to rise more than twice as high within ten minutes following Calurin. Also, these levels persisted higher for at least two hours.[11]

CALURIN is the aspirin of choice, especially when high-dosage, long-term therapy is indicated:

1 High solubility forestalls gastric irritation or damage. This advantage is of special importance in arthritis and other conditions requiring high-dosage, long-term therapy.

2 Produces high salicylate blood levels rapidly for prompt analgesic, anti-pyretic, anti-arthritic effect.

3 Sodium-free — for safer long-term therapy.

4 Flavored: can be chewed or dissolved in the mouth without water if desired — an advantage for patients requiring aspirin administration during the night and for pediatric patients.

Dosage: Each tablet of Calurin is equivalent to 300 mg. (5 gr.) of acetylsalicylic acid. For relief of pain and fever in adult patients, the usual dose of Calurin is 1 to 3 tablets every 4 hours, as needed; in arthritic states, 2 or 3 tablets 3 or 4 times daily; in rheumatic fever, 3 to 5 tablets 4 or 5 times daily. For children over 6 years, the usual dose is 1 tablet every 4 hours; for children 3 to 6 years, ½ tablet every 4 hours, as required. Not recommended for children under 3.

REFERENCES: 1. Waterson, A. P.: Aspirin and gastric haemorrhage, Brit. M. J. 2:1531, 1955. 2. Douthwaite, A. H., and Lintott, G. A. M.: Gastroscopic observation of the effect of aspirin and certain other substances on the stomach, Lancet 2:1222, 1938. 3. Editorial Comments: The effect of acetylsalicylic acid (aspirin) on the gastric mucosa, Canad. M. A. J. 80:47, 1959. 4. Muir, A., and Cossar, I. A.: Aspirin and ulcer, Brit. M. J. 2:7, 1955. 5. Muir, A., and Cossar, I. A.: Aspirin and gastric haemorrhage, Lancet 1:539, 1959. 6. Schneider, E. M.: Aspirin as a gastric irritant, Gastroenterology 33:616, 1957. 7. Bayles, T. B., and Tenckhoff, H.: Salicylate therapy in rheumatic diseases, Scientific Exhibit, Ann. Mtg. A. M. A., San Francisco, Calif., June, 1958. 8. Batterman, R. C.: Comparison of buffered and unbuffered acetylsalicylic acid, New Eng. J. M. 258:213, 1958. 9. Cronk, G. A.: Laboratory and clinical studies with buffered and nonbuffered acetylsalicylic acid, New Eng. J. M. 258:219, 1958. 10. Editorial: Aspirin plain and buffered, Brit. M. J. 1:349, 1959. 11. Smith, P. K.: Plasma concentration of salicylate after the administration of acetylsalicylic acid or calcium acetylsalicylate to human subjects, Report submitted to Smith-Dorsey from Dept. of Pharmacology, Geo. Washington Univ. School of Medicine, Washington, D. C., Sept. 5, 1958.

*TRADEMARK

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pressure rises to a level higher than the diastolic arterial pressure, the arteries show a collapsing pulse with each heart beat. The choroid around the disk may also show atrophy, and in the last stages, at which time the eye is usually blind, the retinal arteries become smaller.

RESPONSIBILITY OF THE GENERAL PRACTITIONER

It is said that if all persons over 40 had their intraocular pressure taken once every three years the incidence of blindness from wide angle glaucoma would drop tremendously. For this reason the general practitioner should suspect all patients over 40 of having this disorder unless proven otherwise, and routinely test them accordingly.

DIAGNOSING WIDE ANGLE GLAUCOMA

The water test is a simple yet reliable method. The intraocular pressure is measured early in the morning after the patient has abstained from food or drink for eight hours. He then drinks a quart of water, after which the pressure is recorded at 15 minute intervals. A rise of 10 mm. of mercury is considered positive. To enable the patient to tolerate measurement of the tension, he is instructed to lie down or lean his head far back, after which two drops of an analgesic are placed in each eye. Any standard instrument may be employed for measuring the pressure, the Schiötz being especially recommended because it is comparatively inexpensive and trouble-free.

TREATMENT

Treatment of this type of glaucoma is preferably medical, the agents commonly employed including pilocarpine, eserine and acetozolamide. If the visual fields continue to lessen despite the use of these agents, surgery is indicated. In prophylaxis it should be remembered that many antispasmodic agents employed for the treatment of gastrointestinal and other systemic conditions, generally have potent mydriatic and cycloplegic effects and therefore may precipitate glaucoma.◀

J. South Carolina M.A., 55:50-52,1959.

Second Attacks of Scarlet Fever: Effect of Penicillin

The effect of penicillin therapy on the occurrence of second attacks of scarlet fever was studied in a series of 7,837 patients, the mean observation time being 6½ years. Early second attacks (within 3 months of the primary infection) occurred in 1.4%. Late second attacks (more than 3 months after the primary infection) occurred in 5%. More than 2 attacks were observed in 0.5% of the patients. The interval between the first and second attacks was less than 2 years in most cases. The likelihood of a second attack was increased when the treatment of the primary attack with penicillin was started before the second day of illness. The tendency to second attacks diminished as age advanced. Despite this observation of an increased incidence of secondary attack in scarlet fever, it is felt that there is no reason to omit or postpone penicillin therapy.

Jansson, E., & Klemola, E., *Brit. M.J.*, 1:1382-1384, 1959.

Experiences with General Anesthesia in Patients with Familial Dysautonomia

Thorough examination, adequate premedication, and careful selection of the anesthetic agents will minimize surgical morbidity among these patients

MARILYN M. KRITCHMAN, M.D., HERMAN SCHWARTZ, M.D., and EMANUEL M. PAPPER, M.D., *New York, New York*

In familial dysautonomia, a congenital condition frequently seen in siblings, all responses to sensory stimuli appear to be either exaggerated or absent. Almost all of the reported patients are small and undernourished. The age of few exceed 20 years, the majority ranging from 1 to 12 years. Many deaths have occurred in the first two to three years of life. The oldest currently is 27 years of age.

The skin blotches are apt to appear with excitement or ingestion of food. Hypertension in response to emotional stimuli is usual. Normal individuals show a slight rise in both systolic and diastolic pressure when changing from the supine to the erect posture. These patients show a fall in systolic and an even more striking fall in diastolic pressure during the same change in posture. All of the reported patients have exhibited postural hypotension.

Especially in the early years, bronchopneumonia and atelectasis are apt to occur, perhaps a consequence of excessive mucoid secretion, or a poor swallowing reflex with aspiration of food or secretions. Even mild infections are accompanied by high fevers which may occur with no overt evidence of infection. Fever and vomit-

ing characteristic of the syndrome often complicate the postoperative period.

The sensory disturbance of importance is indifference to pain, not true anesthesia, since the patients can readily identify pin prick. Diminished lacrimation and corneal anesthesia contribute to the frequency of corneal ulceration. Other characteristics of the disease include poor muscle coordination with absent or hypoactive deep tendon reflexes, dysarthria, emotional lability, and drooling beyond the usual age. Death usually occurs after infection or aspiration of vomitus.

There is no satisfactory treatment. Prefrontal lobotomy, electroshock, tentorial splitting, and lumbar sympathectomy have all failed. Chlorpromazine has proved useful against prolonged vomiting. If given at the onset of an attack in combination with phenobarbital, the vomiting is often stopped and the period of disability seems shortened. Thirteen postmortem examinations have been reported without evidence of consistent or characteristic abnormalities of the central nervous system. Three showed brain lesions; one had a thalamic cyst destroying the dorsal medial nucleus, one had marked degenerative changes in the reticular substance of the pons and medulla, and one had multiple brain abscesses.

Patients with familial dysautonomia are grave anesthetic risks. The labile cardiovascular system, frequent bronchopneumonia, hypersalivation with aspiration, hyperemesis and emotional instability are severe problems for the anesthesiologist. Eight patients with familial dysautonomia received general anesthesia for 27 surgical procedures. Serious morbidity was high. Severe hypotension occurred six times, leading to cardiac arrest twice. Bronchopneumonia was a frequent postoperative complication. All of the cardiovascular problems were associated with the use of thiopental sodium or tribromoethanol (Avertin). As guides to safer management, the following points are suggested:

1. A complete preoperative investigation, including chest x-ray.

2. Premedication with chlorpromazine and a belladonna drug.

3. Use of the volatile anesthetic agents, if local anesthesia after premedication with chlorpromazine is not suitable.◀

J.A.M.A., 170:529-533,1959.

Proteolytic-Antibiotic Ointment for Burns

Severe burns of the eyelids and upper face were successfully treated in 2 cases with an ointment combining wound cleansing properties with antibacterial action. Healing was rapid, with no residual scarring and no need for plastic repair. The ointment (Tryptar) contains trypsin and chymotrypsin, both capable of digesting dead tissue without affecting viable tissue. It also contains bacitracin and polymyxin, making it effective against both gram positive and gram negative bacteria. A special ointment base facilitates application and prevents enzyme loss.

Taub, R. G., *Illinois M.J.*, 114:19-20,1958.

Amenorrhea

A thorough examination will reveal whether the absence of the menses is caused by endocrine imbalance, activity change, or post-operative complications

W. B. GODDARD, M.D., *Iowa City, Iowa*

In any consideration of amenorrhea, secondary or primary, two aphorisms should be stressed:

1. Rule out pregnancy.
2. Make a complete pelvic examination.

Amenorrhea is seen with inanition from any cause, as tuberculosis or glomerulonephritis. A complicated course after any operation may interrupt menstruation until the general condition improves. Obesity alone is a frequent cause. If many a woman will reduce 10 to 15 pounds she will menstruate again. Either hypo- or hyper-thyroidism may cause amenorrhea. The diagnosis must be made before the proper thyroid medication can be prescribed. Pituitary failure is an uncommon cause. Most of these patients have a history of severe blood loss and shock at the time of delivery. The diagnosis may be confirmed on a low pituitary output of hormones. Adrenal hyperplasia, a partial failure of the adrenal cortex to produce cortisone under normal pituitary stimulation, is the cause in some cases. Other causes are the Stein-Leventhal syndrome, early ovarian failure and a number of uterine abnormalities.

Primary amenorrhea may indicate that the patient is not old enough to menstruate. The menstrual history of mother, aunts and sisters may be valuable. Be sure that the patient has no pelvic disease condition. Think

of imperforate hymen and developmental failures, including pseudohermaphroditism. After any sudden change in climate or in activity the menses may disappear for a number of months—evidence for a hypothalamic rather than a nutritional cause.

A complete physical examination and routine laboratory work are necessary, also a careful checking into the regularity of previous periods, together with any family record of abnormal menses or late menarche. A recto-vaginal examination with a well lubricated index finger in the vagina and the middle finger in the anus will give as much information as the ordinary vaginal examination, much more than will a one finger rectal examination. If this approach is not practical, the patient should be examined bimanually under anesthesia and the cervix visualized with a Kelly or a water cystoscope.

Special laboratory tests, including basal temperature graphs and endometrial biopsy, are helpful, particularly in the patient with oligo- rather than amenorrhea. Determination of 17-ketosteroid and pituitary gonadotrophin excretions are expensive, but valuable in many cases.

Patients have been seen with prolonged amenorrhea who developed nausea, tiredness and tenderness of the breasts—due to an early pregnancy. Most gynecologists at some time have had an endometrial specimen examined because of prolonged amenorrhea and have received a diagnosis of decidua of early pregnancy.

Menstruation itself serves no purposeful function. It is wrong to put a patient with undiagnosed amenorrhea on cyclic estrogen, thereby giving her regular periods, unless she understands that this cyclic bleeding will not make her fertile. A specific diagnosis cannot be made in about 40% of patients with amenorrhea. Time and cyclic estrogens may be useful for these patients. Cyclic estrogen with or without progesterone is often given for months in the hope that the ovaries will be stimulated to function cyclically. Natural estrogens seem to have no advantage over stilbestrol. The 19-nor-testosterone compounds (Enovid, Norlutin) are new and expensive and the limits of their usefulness are being explored. They show great promise. X-ray to ovaries or pituitary gland is now considered obsolete. Pituitary hormones are still in the experimental stage. The equine gonadotophins are available commercially but in our present knowledge have no uses.◀

Mississippi Valley M.J., 81:123-124,1959.

Childhood Nephrosis

Comparison of various types of treatment used for 65 children (comprising an approximately homogenous group) with nephrosis of unknown origin showed that corticosteroid therapy was the only treatment having a pronounced effect. The children adequately treated with these hormones showed an appreciably lower mortality rate during the first 5 years and were able to lead normal or almost normal lives. They were given hydrocortisone (150-200 mg. daily) or 30 to 40 mg. prednisone daily 3 days a week for 9 to 15 months.

Hiekkala, H., et al., *Ann. paediat. Fenniae*, 5:16, 1959.

Toxic Effects of Digitalis and Quinidine

Either of these agents is capable of producing arrhythmias if administered incorrectly

ARNOLD S. MOE, M.D., *East St. Louis, Illinois*

These drugs usually are safe when prescribed in proper dosage and with certain precautions. Digitalis, quinidine and antihypertensive drugs—with salt-free diets and diuretics—may be required for months, years, or a lifetime.

In many cases the maintenance dose is the cause of toxic effects, although this dose fits most patients. Each case must be strictly individualized.

The causes of digitalis intoxication are: inaccurate history, inflexibility, confusion, and hurry. Patients have been given large doses of a form of digitalis by two different physicians on the same day. The margin between therapeutic and toxic doses narrows as the severity of heart disease increases, and potassium ion depletion renders the heart much more sensitive to digitalis. Confusion comes from indiscriminate use of digitalis preparations, the mixing of many drugs into one dose, or the giving of many separately in rapid succession.

In cor pulmonale, never use rapid digitalization lest pulmonary arterial pressure increase too rapidly. In the first place its use may or may not help. This applies equally to cases of mitral stenosis of severe degree in whom pulmonary edema may be precipitated. Digitalis must not be pushed to intoxication in an attempt at slowing the rate. Thyrotoxicosis fibrillation may be helped without slowing the rate. A daily dose of 0.2

mg. digitoxin has proved toxic and single-dose full digitalization often results in toxicity with any kind of digitalis preparation.

Practically all types of arrhythmia may be so produced. In a group of 100 such patients, seven of 27 deaths were due to digitalis intoxication. Signs of toxicity following vigorous diuresis are due mainly to potassium depletion and if this depletion already exists or is suspected in a previously edematous patient, digitalis must be used with extreme care. In case of arrhythmia disappearing after digitalization and then reappearing, or increase in rate previously well controlled during maintenance therapy—withhold digitalis for two or three days before increasing the dose. Be wary of cases with previously irregular rhythm, changing to a regular rhythm, but at an increased rate. The importance of the potassium ion is becoming more evident.

Digitalis may be prescribed overenthusiastically. A tachycardia of 94, with extreme prolongation of the AV conduction, is evidence of severe digitalis intoxication, especially when several weeks after stopping digitalis the pulse had dropped to 65. Toxic effects of digitalis do not always go on from anorexia, nausea, and vomiting to more severe symptoms.

Quinidine, a drug used in the treatment of cardiac arrhythmias, may give rise to many toxic symptoms ranging from mild to lethal. One advantage over digitalis is its noncumulative effect; a distinct disadvantage lies in the fact that a single small dose may be followed by cardiac arrest or respiratory failure.

Quinidine tends to produce ventricular arrhythmias as a complication of the treatment of atrial arrhythmias or premature ventricular contractions. On the other hand, it has long been used as an effective treatment of ventricular dysrhythmias. Ventricular tachycardia responds very well to quinidine therapy, and is considered almost a specific drug for this type (ventricular) of tachycardia. Ventricular tachycardia may be caused by quinidine as an idiosyncrasy to the drug.◀

Illinois M.J., 115:334-341,1959.

Parotitis Following Diuretic Therapy

Suppurative parotitis usually arises from a retrograde invasion of the gland by oral bacteria. Confirming diagnostic signs include dehydration and a reduced flow of saliva from the gland. Attention to fluid and electrolyte balance during surgery successfully prevents dehydration in these cases.

A form of parotid gland infection described as "medical parotitis" consists of an otherwise ordinary suppurative parotitis complicating administration of chlorothiazide and mercaptomerin. Observation of this condition in 5 patients suggests that vigorous dehydrating measures, even in the face of persistent edema, must always be attended by careful observation of fluid intake.

Power, L., *New England J. Med.*, 260:1079,1959.

Early Treatment of Intracranial Aneurysms of the Circle of Willis

Good results may be expected in otherwise healthy patients if surgical correction quickly follows diagnosis

J. L. POOL, M.D., *New York, New York*

An intracranial aneurysm, or any other, may rupture at any moment. Therefore surgical treatment should follow the diagnosis of aneurysm as soon as possible. The timing and type of surgical intervention will depend largely on the age and condition of the patient, and the location and character of the aneurysm. Most of these aneurysms are of congenital saccular or berry type that arise from the circle of Willis, or more rarely from its peripheral branches or the vertebral-basilar arteries. There is a 13% incidence of multiple aneurysms.

Clinical indications are first apt to become evident between the ages of 30 and 60 years. Subarachnoid hemorrhage, usually the first evidence of such an aneurysm, is manifested by sudden violent headache followed by nuchal rigidity and lethargy. Photophobia, striate retinal hemorrhages and coma may also develop. Lumbar puncture reveals a bloody cerebrospinal fluid, usually under increased pressure. In a third of proven intracranial aneurysms, subarachnoid hemorrhage is not a presenting symptom and may never occur if appropriate treatment is promptly instituted. The diagnosis and location of an aneurysm may be suggested by focal symptoms, such as intermittent

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unilateral headaches, often resembling migraine, or retro-orbital pain followed by ptosis, pupillary dilation and oculomotor weakness.

Contralateral seizures, hemiparesis, or reflex and sensory signs are more apt to be associated with an aneurysm of the middle cerebral artery, while visual field changes similar to those associated with pituitary tumors, and mental confusion, may be caused by an aneurysm of the anterior communicating artery. Aneurysms elsewhere, including those of the vertebral-basilar system, usually result in symptoms and signs clearly pointing to their location.

It is important to note that contralateral hemiplegia, abnormal sensory and reflex signs, or mental obtundity may also be due to regional or remote circulatory insufficiency of the brain caused by the cerebral vasospasm, that so frequently develops within a few hours or days after an intracranial aneurysm has ruptured. Progression of any of these signs may indicate hematoma formation, serious extension of cerebral vasospasm, or an enlargement of the aneurysm sac that threatens imminent rupture. Immediate surgical intervention is thus all the more urgent.

Cerebral angiography by the carotid route, now relatively safe, is essential whenever an intracranial aneurysm is suspected. Bed rest without surgical intervention can no longer be regarded as proper treatment for intracranial aneurysms except for the very ill, comatose or elderly patient unable to tolerate an operation. Without surgery the combined immediate and ultimate mortality rate for rupture is at least 50% and has been reported as high as 87%.

Early intracranial surgery for the treatment of aneurysms of the circle of Willis or its branches is indicated, preferably within six days after presenting symptoms, whenever the age and the condition of the patient permit. Satisfactory results may be expected in patients below 50 years of age who are in reasonably good physical condition, less good results in patients over 50 and poor results in those who are comatose, regardless of their age. Special removable clips for temporary local intracranial reduction of blood flow at the site of the aneurysm facilitate aneurysm surgery, particularly for the isolation and permanent obliteration of recently bleeding anterior communicating artery aneurysms. Despite the value of this technique its application is not advocated in every case of intracranial aneurysm. Each patient is treated according to the method deemed most suitable for his particular case.◀

Bull. New York Acad. Med., 35:357-369,1959.

Penetrating Wound of Both Frontal Lobes By a Ski Pole

Clinical aspects of the successful recovery of a patient following an unusual accident are presented and discussed

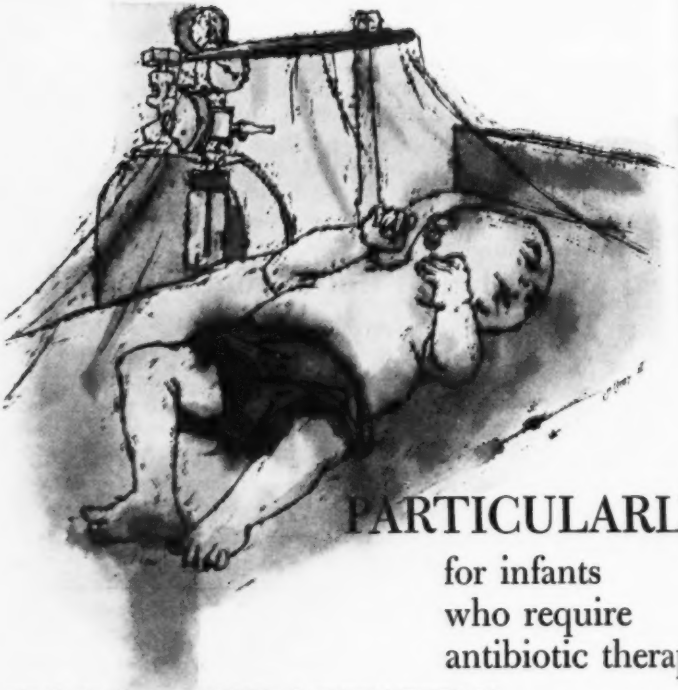
ERNEST SACHS, JR., M.D., *Hanover, New Hampshire*

The famous crowbar* case of Phineas Gage of a century ago is not without its occasional parallels in present-day medicine. Head injuries as a result of skiing are uncommon, although skull fractures, extradural hematomas, concussions and subdural hematomas occur, and some necks have been broken in skiing.

A boy of 15 was admitted to the hospital two hours after having been found on a ski slope with the blunt end of an uncovered bamboo ski pole sticking forth from the right cheek, just inferior and lateral to the corner of the mouth. It was reported that he was conscious and oriented, but drowsy, the pupils were equal, he was able to move all extremities, had bilateral Babinski reflexes. X-ray examination with the ski pole in place showed it to have penetrated 20 cm. through the right cheek, across the midline into the left frontal lobe just beneath the calvarium. With a twisting motion the pole was slowly removed, without incident.

He was immediately transferred to another hospital, upon admission he gave his name, age and address, but fell asleep between questions. He complained of no pain. The pupils were equal, the fundi normal. There

*Actually tamping rod.—*Editor.*



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Oral Suspension (orange-pineapple flavor) 2 oz. bottle, each tsp. (5 cc.) contains 125 mg. Cosa-Tetracyn® plus 125,000 u. nystatin

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was vision in each eye. There was no cerebrospinal-fluid rhinnorrhea. Reflexes were symmetrically equal and active. Strength was good in both arms and both legs. He had bilateral extensor plantar responses. X-rays showed the course of the 1.3 cm. pole to have been through the right maxillary sinus, the right ethmoid sinus and the medial wall of the right orbit, through the cribriform plate into the right frontal lobe, across the midline into the left frontal lobe, where a small fragment of bone was visible at the end of the pole just beneath the calvarium. A piece of bone and a core of brain biopsy were found in the end of the bamboo pole, which had been sent with the patient. The wound of entrance was debrided and carefully sutured, and 1,000,000 units of penicillin given every six hours, and 2.5 gm. of sulfadiazine I.V. and streptomycin 0.5 gm. twice a day.

For 24 hours he was lethargic, restless and turning about in bed. He vomited a number of times and was incontinent of urine. After 24 hours the blood pressure of 140/90 began to rise and reached 180/80, with respirations of Cheyne-Stokes quality. The left pupil became dilated and fixed. He began to assume a decerebrate posture. In the operating room, under general anesthesia and I.V. administration of 30% urea (1 gm. per Kg.), bifrontal craniotomy was carried out. This revealed the wound of entrance as through the roof of the right orbit, transecting the *right* frontal lobe far anteriorly, passing into the *left* frontal lobe in front of the corpus callosum and the anterior cerebral arteries. No significant hemorrhage was found. The main problem was that of edema, which was controlled with urea I.V.

Immediately after operation the decerebrate posture disappeared, pupils were equal and reacted normally. Urea was given I.V. every 12 hours for the next two days to control the increased pressure; thereafter it was unnecessary. The wound healed well by first intention. The rectal temperature reached 103°F. at the highest, was normal by the 4th postoperative day when the patient began to answer questions and the Babinski responses disappeared. He was out of bed in a chair on the 8th day, discharged on the 17th, when a slight diplopia was his sole complaint. Intellectually and emotionally he appeared normal to all observers, including parents and friends. Five months later he appeared normal and was doing well in school.◀

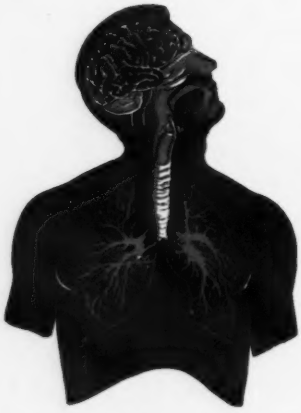
New England J. Med., 260:1333-1334,1959.

Stein-Leventhal Syndrome

This syndrome is characterized by oligomenorrhea or amenorrhea, sterility, bilaterally enlarged ovaries with small cysts, and in many cases male hair distribution. Clinical and histological data from 8 typical cases demonstrate that it is of 2 types, in the first of which the ovaries are functional and the source of the masculinizing factor, and in the second of which the ovaries are not functional, the masculinizing factor apparently being derived from the "sexual zone" of the adrenal cortex acted upon by pituitary gonadotropin.

Pesonen, S., et al., *Acta endocrinol.*, 30:405,1959.

the addition of the decongestant makes for better cough control



by decongesting the cough area

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TRIAMINICOL provides more complete cough control than regular "cough syrups" because it contains Triaminic,[1,2,3] the leading oral nasal decongestant. This decongests the mucous membranes of the respiratory tract, reducing swelling and sensitivity, and controlling irritating postnasal drip, a common cough stimulus.

TRIAMINICOL also acts directly on the cough reflex center. It provides the nonnarcotic antitussive, Dormethan, fully as effective as codeine but without the drawbacks of codeine.[4] Liquefaction and expulsion of exudates is aided by the classic expectorant action of ammonium chloride.

Each 5 ml. tsp. of TRIAMINICOL provides:

Triaminic®	25 mg.
(phenylpropanolamine HCl	12.5 mg.
pheniramine maleate	6.25 mg.
pyrilamine maleate	6.25 mg.)
Dormethan (brand of dextromethorphan HBr)	15 mg.
Ammonium chloride	90 mg.

In a pleasant-tasting, fruit-flavored, non-alcoholic syrup.

Dosage: Adults – 2 tsp. 3 or 4 times a day; children 6 to 12 – 1 tsp. 3 or 4 times a day; children under 6 – dosage in proportion.

References: 1. Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. 2. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 3. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958. 4. Bickerman, H. A.: in Drugs of Choice, Mosby, St. Louis, 1958, p. 547.

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Religious Symbolism and the Pharmacology of Peyote

Psychiatrists are becoming interested in the hallucinogenic aspects of a mushroom which has been used since the pre-Columbian era

FRANCES KELSEY, M.D., *Vermillion, South Dakota*

In recent years the use of peyote in the religious ceremonies of the Native American Church has been a subject of controversy between those who advocate the abolition of such pracitces on medical or moralistic grounds and those who believe the doctrine of religious freedom prohibits such legal recourse. A group of anthropologists (LaBarre et al.) have made extensive studies of peyotism in various Indian tribes and decided that peyote is used sacramentally "in a manner corresponding to the bread and wine of christians."

The Aztecs called peyote "the flesh of the gods" long prior to the arrival of the Spaniards. The belief that those who ate of this "flesh" would behold the world of the gods is creditable in the light of the present knowledge of the drug's actions. For over 300 years the use of peyote has been ecclesiastically banned although secretly enjoyed; it was gradually absorbed into the Christian dogma of certain Indian groups, being considered the flesh of Christ and nourishment for the soul.

In a monograph on peyote, published in 1928, (Kluver) quotes Weir Mitchell's classic description: "The display which for an enchanted two hours followed was such as I find it

hopeless to describe in language which shall convey to others the beauty and splendor of what I saw. Stars . . . delicate floating films of colour . . . then abrupt rush of countless points of light swept across the fields of view . . . zigzag lines of bright colours . . . the wonderful loveliness of swelling clouds of more vivid colours, gone before I could name them . . . All the colours I have ever beheld are dull in comparison to these." In his last vision Mitchell saw a beach with its rolling waves as "liquid splendours, huge and threatening, of wonderfully pure green, or red or deep purple, once only deep orange—and with no trace of foam."

Peyote (Lopophora Williamsii) is a small carrot-shaped cactus which grows in the Southwest. The top is cut off and dried, forming the "peyote button." Portions of these are eaten until the desired effects are obtained. Peyote's principal ingredient is completely responsible for the extraordinary visions of the peyotist. One ounce of the crude drug would contain 270 mg. of mescaline, an amount adequate for profound effects in most individuals. Single oral doses of 100 or 200 mg. of mescaline may be expected to produce mydriasis, sweating, and an increased amplitude of the knee jerk. Postural reflexes may be affected. With larger doses, the earliest effects are nausea and vomiting, palpitation and restlessness; coarse tremors may appear, first in one extremity then another, and sometimes in all four and the head and neck. The experience is considered pleasant by many, but some have found it very disagreeable and refuse further use of the drug.

The disturbance in mental function differs from that from cocaine, marihuana and morphine. Mescaline might be added to the classic story of the reactions of the several drug users who suddenly died and went up to heaven. Finding their way barred by the pearly gates, the cocaine-addict banged his way through, the hashish-eater floated over, and the morphine-addict quietly went to sleep. The peyotist presumably sat quiet, lost in a vague cloud of the flashing brilliances of colors from the gates.

The dramatic effects of mescaline on color vision has prompted studies of the locus of this effect. Persons who have become blind in adult life will relate experiences indicative of the usual "indescribably beautiful" color patterns, which seem to appear first in the eye which became blind last. Persons born blind, or who lost their vision very early in life and have no previous appreciation of colors, experience great distortions of acoustic, tactile and thermal sensations. The mescaline hallucinations must therefore involve more complex neural integration than simply peripheral receptors, although these certainly trigger the phenomona. Most writers describing their experiences have mentioned the intensification of visual imagery when the room is darkened or lit only by flickering fire as well as the precipitation of new hallucinations by delicate stimuli for the senses of feeling, hearing, smelling or tasting. Thus the essence of the action of mescaline is aberrant interpretations of common environmental stimuli.◀

South Dakota J. Med. & Pharm., 12:231-233, 1959.

Intestinal Angina Diagnosed Preoperatively And Relieved Surgically

This abdominal syndrome is discussed and the successful treatment of a single case is presented

WILLIAM P. MIKKELSEN, M.D., and
JOHN A. ZARO, JR., M.D., *Los Angeles, California*

Intestinal angina is a syndrome that may precede the acute abdominal catastrophe of ischemic bowel infarction, at which stage death is usually inevitable. A review of the U.S. literature suggests that this prodrome has been suspected during life in only two recorded cases. In each of these, the conclusive diagnosis was established only at emergency surgery for bowel infarction. It is believed that this disease frequently occurs but has been consistently overlooked.

The syndrome may exist for weeks, months or years before complete occlusion of the mesenteric artery occurs. It is consistently characterized by cramping abdominal pain, perhaps with radiation to the back, or a sense of distention or bloating with a constant abdominal ache, usually developing 15 to 30 minutes after eating and lasting one to three hours. Its severity and duration depend upon the amount and character of food ingested. Progression of symptoms is steady. Nausea, vomiting and diarrhea may occur. "Food pain" soon leads to a reluctance to eat. Weight loss follows. Physical, laboratory and x-ray examinations are negative. The cause is atherosclerotic obliteration

or narrowing of the ostia of gastrointestinal branches of the abdominal aorta. Collateral anastomoses maintain intestinal viability and function when one of these branches becomes completely occluded.

A retired pipefitter of 62 years, first hospitalized because of abdominal pain and vomiting, suffered abdominal pain after most meals for two years, occasionally relieved by vomiting. Pain was described as squeezing and bloating. Several medications had been used without benefit. Constipation had existed for years, and the patient had lost 40 pounds. Pain in the left hip, thigh, and calf, developed after walking two blocks, was relieved by rest. Further past history and family history were noncontributory.

A bland diet with anticholinergics appeared beneficial. After one month postcibal distress became inconstant, there was a weight gain of 5 pounds. He was discharged with a diagnosis of abdominal pain of unknown etiology. At home these episodes continued and the constipation became more severe, passage of flatus sometimes providing relief. A steady increase in the frequency and severity of pain led to progressive reduction in the size of his meals, and a year later he was hospitalized. His weight at this time was 122 lbs., three years previously it had been 175 lbs. A systolic bruit was audible over the upper abdomen, and aortic pulsations were palpable in epigastrium to 1 inch above the umbilicus. Iliac, femoral, popliteal and pedal pulsations were absent bilaterally. There was an increase in abdominal wall arterial collateral circulation. Suspicion of intestinal angina was strong, and the abdomen was opened. Aortic occlusion started just below the renal arteries and extended to the external iliacs bilaterally. The inferior mesenteric artery was occluded, the superior mesenteric and its intestinal branches being pulseless. A thrill was palpable in the hepatic, left gastric, and splenic arteries, but there was no expansile pulse. There was a great increase in extraperitoneal collateral arterial circulation.

The superior mesenteric artery, collapsed and pulseless, was mobilized 5 cm. from its origin, and as the dissection was carried cephalad the artery was found firmly encased in cicatricial tissue. Dissection of the first 4 cm. of the artery was completed, its origin with the aorta cleared, and a strong pulsatile blood flow developed through this previously collapsed vessel. At the ostium and for 5 cm. there was incomplete atherosclerotic obstruction. A 1.5 cm. longitudinal arteriotomy was made 3 cm. from the origin and 20 mg. heparin instilled into the distal segment of the superior mesentery. A 2 mm. probe was the largest that would pass through the ostium into the aorta. After closure of the arteriotomy, vigorous pulsations returned to this artery and its mesenteric branches.

During the next two months the patient gained 8 lbs., the symptoms were completely relieved, and there was no postcibal distress. Anticoagulant therapy started a few days postoperatively was maintained.

Six cases of intestinal angina have been identified in the last two years, only the case reported being recognized before the onset of intestinal gangrene. Complete symptomatic relief follows surgical correction.◀

New England J. Med., 260:912-914,1959.

Spontaneous Abdominal Paracentesis

A man of 47 was admitted to hospital because of the development of ascites. At paracentesis 6000 cc. of amber fluid was withdrawn. The patient was discharged on a high-protein, high-calorie diet, with vitamin supplements. He subsequently had several admissions to other hospitals for paracentesis.

He was readmitted to hospital 1 year later with leakage of fluid from the abdomen. Nine months previously he had developed an umbilical hernia, which had grown larger. For several weeks he had noted increasing abdominal distention and ankle edema. The night of admission he felt a trickle of fluid on his abdomen and fluid leaking from the hernia. He had also developed an inguinal hernia on the left. His psoriasis was in exacerbation. The total protein level was 5.5 gm.%, with an albumin-globulin ratio of 3.0/2.5. He remained afebrile, and the drainage was allowed to continue freely. Penicillin and streptomycin were given prophylactically. Three days later an umbilical herniorrhaphy was done under local anesthesia (procaine), and a polyethylene tube inserted through a stab wound for drainage. The postoperative course was uneventful, and the drainage continued. After the tube was withdrawn, his abdomen began to distend with fluid. He was seen one month after discharge in the outpatient clinic, his wound was well healed but his abdomen much distended with fluid. He did not return for follow-up.

Lerner, S. & Rost, M. S., *J.A.M.A.*, 170:1310-1311, 1959.

Effect of Hypercalcemia Induced by Calciferol upon Renal Concentrating Ability

Patients with hypercalcemia have frequently shown polyuria and loss of ability to concentrate urine. The effects of hypercalcemia on renal function and morphology were studied in rats given large doses of calciferol for several days—4 daily injections of 200,000 to 400,000 units. The result was marked impairment of ability to concentrate urine, little or no change in blood urea, urea clearance, or excretion of phenolsulfonphthalein. Changes in the anatomy of the kidneys were few, and consisted chiefly of lesions of the collecting duct in the outer medula. It is suggested that similar alterations in structure and function of the kidneys may be responsible for the urinary changes observed in a variety of urinary states associated with hypercalcemia or nephrocalcinosis.

Epstein, F. H., et al., *J. Clin. Invest.*, 37:1702-1709, 1958.

Vascular Headache

There are three well-recognized stages of vascular headaches:

1. Vasoconstriction, during which the patient may experience aurae or prodromal symptoms including visual changes, scintillating scotomata, or mood changes.

2. Vasodilation, in which the pain is due to an increased amplitude of pulsation producing afferent impulses on nerve tendrils in the vessel walls. During this stage visual changes may persist and nausea and vomiting occur.

3. Edema, occurring in the artery wall if dilation of the artery continues.

Causes may be precipitating, predisposing, or a combination of the two. Precipitating causes include temperature changes, hunger, fatigue, allergic reactions, excessive smoking, emotional episodes, toxic states, vasodilator substances, biochemical changes and nerve irritation. Predisposing factors are mechanical lesions of the cervical spine, unmarried state, occupation, hypertension, nasal abnormality, sex, heredity, age, advanced education, psychogenic states and nasal allergy. Both precipitating and predisposing factors are endocrine, nasal and biochemical changes, eyestrain, mental conditioning, stress, and medical pathology.

Depending upon predisposing and precipitating factors, effective prophylactic therapy includes tranquilizers, Bellergal, antihistamines, nose drops, and steroids administered as a nasal spray. Histamine injections may induce a refractory state in which the patient remains asymptomatic. Since the pain of vascular headache is due to dilation of certain blood vessels, general vasoconstrictors such as epinephrine, methylisoctenylamine, or ergotamine tartrate are indicated in symptomatic treatment. The last preparation is usually effective parenterally in a dose of 0.25 mg. Wigraine, an oral combination containing ergotamine tartrate, caffeine, 1-belladonna alkaloids and acetophenetidin (Wigraine), has also been effective in controlling symptoms. Dosage is one to two tablets every half hour for a total of six tablets, the maximum weekly dosage being 12 tablets. Levorotatory alkaloids of belladonna are especially useful in patients with associated nausea and vomiting, while a non-narcotic analgesic such as acetophenetidin relieves muscle spasm frequently accompanying or following the headache. Narcotics such as codeine or demerol are not ordinarily indicated.

Ogden, H. D., *J. Louisiana M.S.*, 110:390-395,1958.

Esophageal Hiatal Hernia

This abnormality, capable of causing signs and symptoms suggestive of other disorders, was found in 51 (7.9%) of 638 consecutive x-ray studies of the upper gastrointestinal tract. Case records of 49 available for study revealed the following:

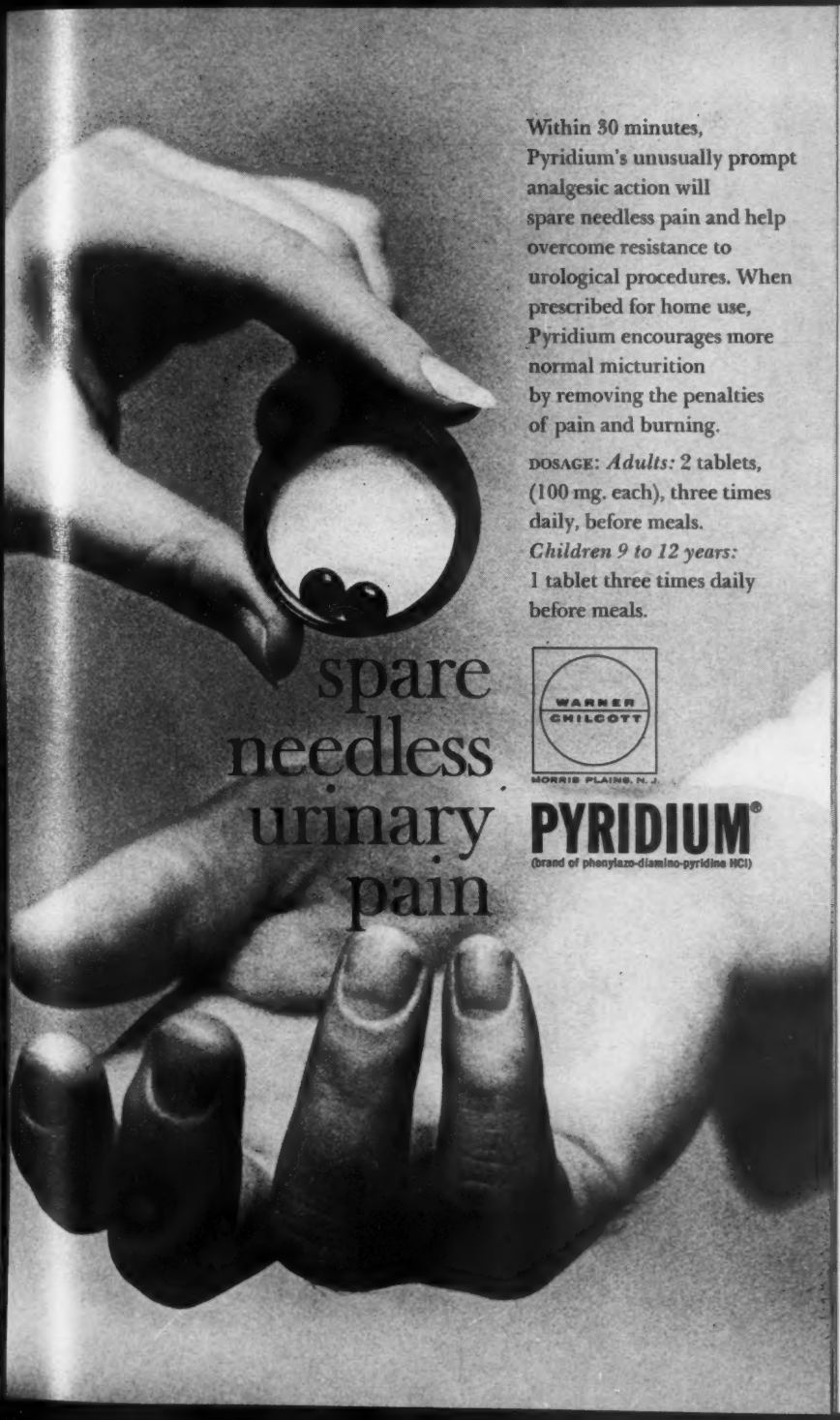
1. Relative incidence was slightly higher in males than in females.

2. Obesity was found in 33 (59% of the males, 82% of the females).

3. About 87% of the males were coal miners, suggesting that hard physical labor and pulmonary disease may be etiologic factors.

4. Presenting complaints could be related to the hernia in about 50%.

5. In 16 cases (about 33%) the chief complaint suggested heart disease. In only 5 were there definite signs of



Within 30 minutes, Pyridium's unusually prompt analgesic action will spare needless pain and help overcome resistance to urological procedures. When prescribed for home use, Pyridium encourages more normal micturition by removing the penalties of pain and burning.

DOSAGE: *Adults:* 2 tablets, (100 mg. each), three times daily, before meals. *Children 9 to 12 years:* 1 tablet three times daily before meals.

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myocardial damage.

6. Symptoms suggestive of hiatal hernia (in the order of highest frequency) were heartburn, precordial pain, dysphagia, epigastric pain and left shoulder pain.

7. Of the 49 hernias, 45 were esophagogastric (33 small or sliding, 11 moderate, 1 large) and 4 were paraesophageal. Type of hernia could not be related to nature or severity of symptoms.

8. Medical therapy was successful in controlling symptoms in all but 6. Complications such as esophagitis, ulcer, hemorrhage, stricture or uncontrollable pain may require surgical treatment.

Willard, J. H., & Dossett, B. E., *J. Kentucky M.A.*, 56:653-659,1958.

Office and Bedside Estimation of Pulmonary Function

It is sometimes necessary to determine whether dyspnea has its origin within the lungs or elsewhere. An assessment of pulmonary function should be a part of every general examination of a patient who has had serious pulmonary disease or who is in middle or late life. A good assessment of pulmonary function can be made in the office.

In recent years the time-honored and simple test of vital capacity has fallen into an undeserved disrepute because of enthusiasm for complex and exact tests devised by physiologists. The two elements needed to assess ventilatory function are usable ventilatory volume (vital capacity) and the ease with which the subject can ventilate this space. Only parts of the lungs which can be emptied quickly are useful under circumstances of exertion.

For determination of vital capacity, one can use a BMR machine (and obtain a written record of the effort), or a water-filled vital capacity apparatus. These methods are cumbersome for the office or hospital ward.

The McKesson-Scott Bellows Vital Capacity Apparatus costs about the same as an aneroid sphygmomanometer. This machine has no device to measure air expelled in the first second, but it is satisfactory to record the total quantity expelled and the speed of expiration. Thus a normal healthy man might have a vital capacity of 4.5 liters rapidly expelled, recorded as V.C.=4.5 l (fast). A recording of 4.0 l (slow) would indicate slowing of expiration with total lung capacity little changed. A value of 2.0 l (fast) would indicate a restriction of lung expansion but an airway free of obstruction, and perhaps little dyspnea.

It is suggested that the physician walk with the patient on level terrain and up at least one flight of stairs while encouraging the patient to talk. One can maintain a conversation while walking only when he can comfortably excrete the carbon dioxide while breathing at a rate suitable for speech. The onset of dyspnea is indicated by the patient's talking in shorter phrases with quick expiration and inspiration between phrases and finally a reluctance to talk at all.

A stoic may deny dyspnea, yet not be able to talk while walking. A psychoneurotic patient may complain bitterly of various symptoms while walking up several flights of stairs.

Simple tests of ventilation with a good history and physical examination will solve most practical problems of pulmonary function.

Stead, W. W., *J. Florida M.A.*, 45:1285-1289,1959.


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The Unheard Diastolic Murmur in Acute Rheumatic Fever

A crucial feature in the clinical diagnosis of rheumatic heart disease is the demonstration of certain cardiac murmurs. Since these murmurs can exist with or without other abnormalities, laboratory and other data or a positive history, the major diagnostic procedure in rheumatic heart disease is auscultation.

The 359 patients previously free of rheumatic heart disease had had acute attacks of rheumatic fever that unequivocally fulfilled the modified Jones diagnostic criteria. The acute stage of the disease had passed in a majority. All auscultatory data were examined to determine the frequency of the two types of murmurs during the acute rheumatic attack: an early, high-pitched, blowing diastolic murmur at the base or left sternal border; and a soft, mid-diastolic apical murmur, with an apical systolic murmur.

In some cases a diastolic murmur noted at the referring source persisted, in others it disappeared before transfer. In some, a diastolic murmur was found on admission, not previously noted. Since most of the patients no longer had active rheumatic fever, and the interval since last examination was brief, these murmurs had presumably been present during the earlier examinations elsewhere but had not been recognized.

In 230 patients no diastolic murmurs were found during or immediately after the acute rheumatic attack. In 14, diastolic murmurs were noted at some time after admission. In the remaining 115 diastolic murmurs were detected before or upon admission.

These had not been previously recognized in 27% (31 of 115) of all patients who had them. Thirteen teaching hospitals had referred 46 of these patients; in 4 of this group (9%) the murmur was unheard. The 69 patients from non-teaching sources had come from 39 different hospitals, clinics or private physicians. In 27 of these patients (39%) the diastolic murmur had been undetected. These unheard diastolic murmurs in the 31 patients were located in the following areas: basilar or left sternal border, 15; apical, 15; and both, 1.

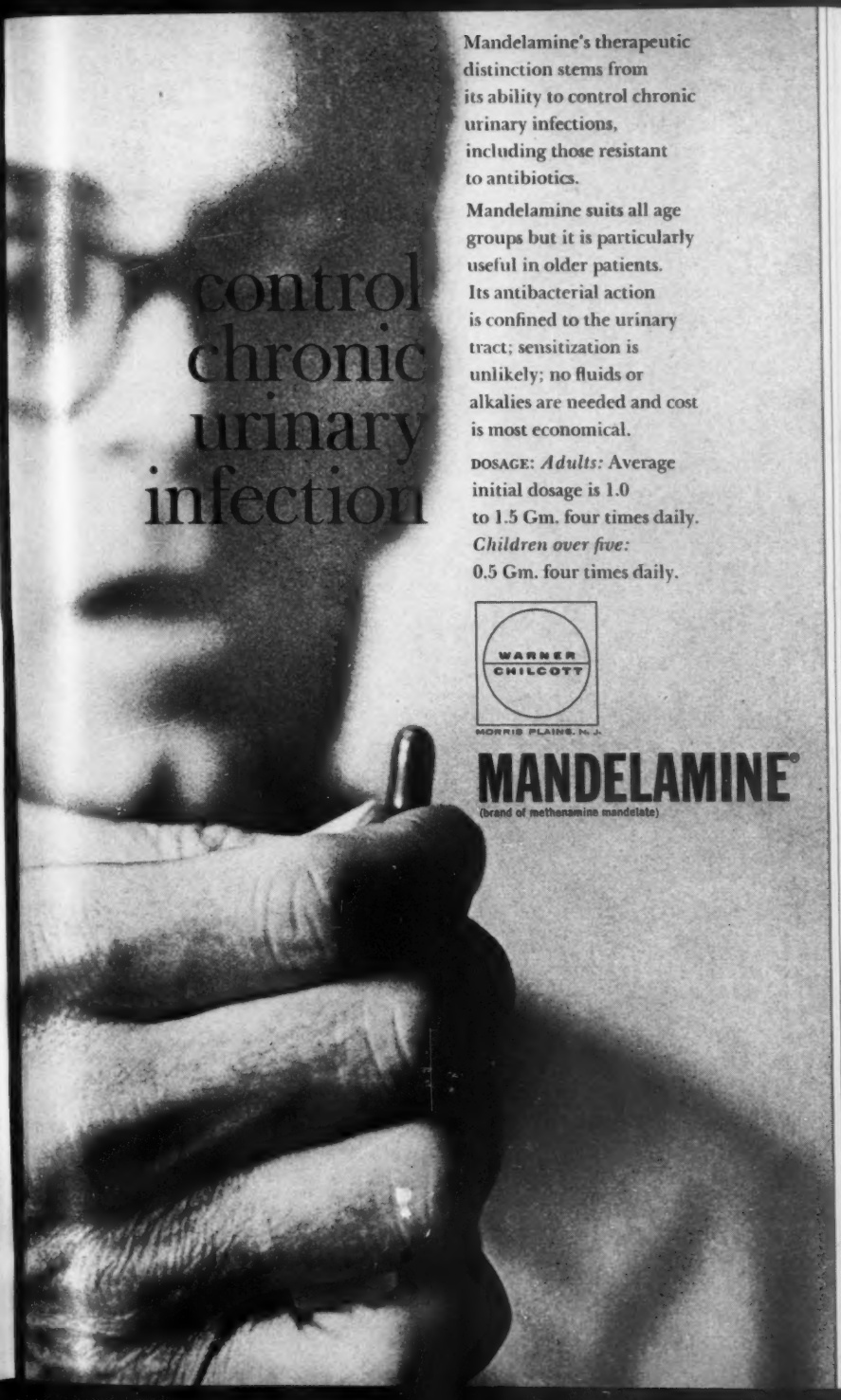
Diastolic murmurs appeared during the acute or early convalescent phase of rheumatic fever in 129 of 359 patients without previous rheumatic heart disease. In 14 patients, the murmurs were detected after the patient was transferred, in 115 they were noted previously or on admission. In 31 of the 115 patients in the latter group, the murmurs were first found only upon admission. It was evident that these murmurs had existed without being identified at the previous medical source. These "unheard" murmurs had occurred in 9% (4 of 46) of patients referred from teaching hospitals, and in 39% (27 of 69) of those referred from other sources.

If these murmurs are not noted during the acute rheumatic attack, they may be found at later examinations, and erroneously attributed to new conditions.

Feinstein, A. R., & Di Massa, R., *New England J. Med.*, 260:1331-1333,1959.

Moles and Melanomas

The mole is constantly available for study, the melanoma the most accessible of all malignant tumors. One thousand adult patients who came to a general diagnostic clinic with no concern about their moles were ex-



Mandelamine's therapeutic distinction stems from its ability to control chronic urinary infections, including those resistant to antibiotics.

Mandelamine suits all age groups but it is particularly useful in older patients. Its antibacterial action is confined to the urinary tract; sensitization is unlikely; no fluids or alkalies are needed and cost is most economical.

DOSAGE: *Adults:* Average initial dosage is 1.0 to 1.5 Gm. four times daily. *Children over five:* 0.5 Gm. four times daily.

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amined to ascertain the distribution and character of their nevi. This study revealed that the average patient has 15 moles, or true nevi, and that they, as distinguished from pigmented spots, are scarce on the feet and genitals. In 1,225 patients, it was found that the melanoma was very frequent on the soles and quite common on the genitals, in contra-distinction to the general distribution of pigmented moles. The conclusion which can be drawn from this comparative analysis is that certain moles occurring on the feet and genitals present a greater hazard than other kinds occurring elsewhere. The junctional nevi, which are most inclined to become melanomas, are three times as frequent on the feet as on other skin surfaces. The lesson to be learned from such knowledge is the advisability of surgical excision of such pigmented moles occurring in these locations.

Malignant melanomas occur most frequently in blonds, particularly those who have extremely pale skins of soft texture, but including those of sandy complexion, and those with red hair who may freckle easily but do not tan well. The prognosis is extremely bad in this type. The routine removal of all brown or black moles in blonds or red-heads of the skin coloration described is urged. Simple excision or excisional biopsy with primary wound closure is sufficient for moles that appear benign. All moles of suspicious or dangerous character should be removed before the advent of puberty.

Microscopic study of every pigmented mole that is excised should be made. A malignant melanoma may have multiple primary foci in the same individual. Many pigmented nevi are not visible until after the onset of puberty. There is obvious necessity for complete surgical removal in childhood of all dark, deeply pigmented nevi.

It is not always possible to detect metastases in the early stage, or to know by which of the vascular routes cells will be disseminated. Those malignant melanomas which seem to metastasize via the lymphatics are still amenable to surgical treatment; those which enter the blood early are apt to be incurable.

One hospital's five-year cure rate for all patients with malignant melanomas treated during 1917-1945 was 21.4%. During 1948-1951, the five-year cure rate was 37.9%.

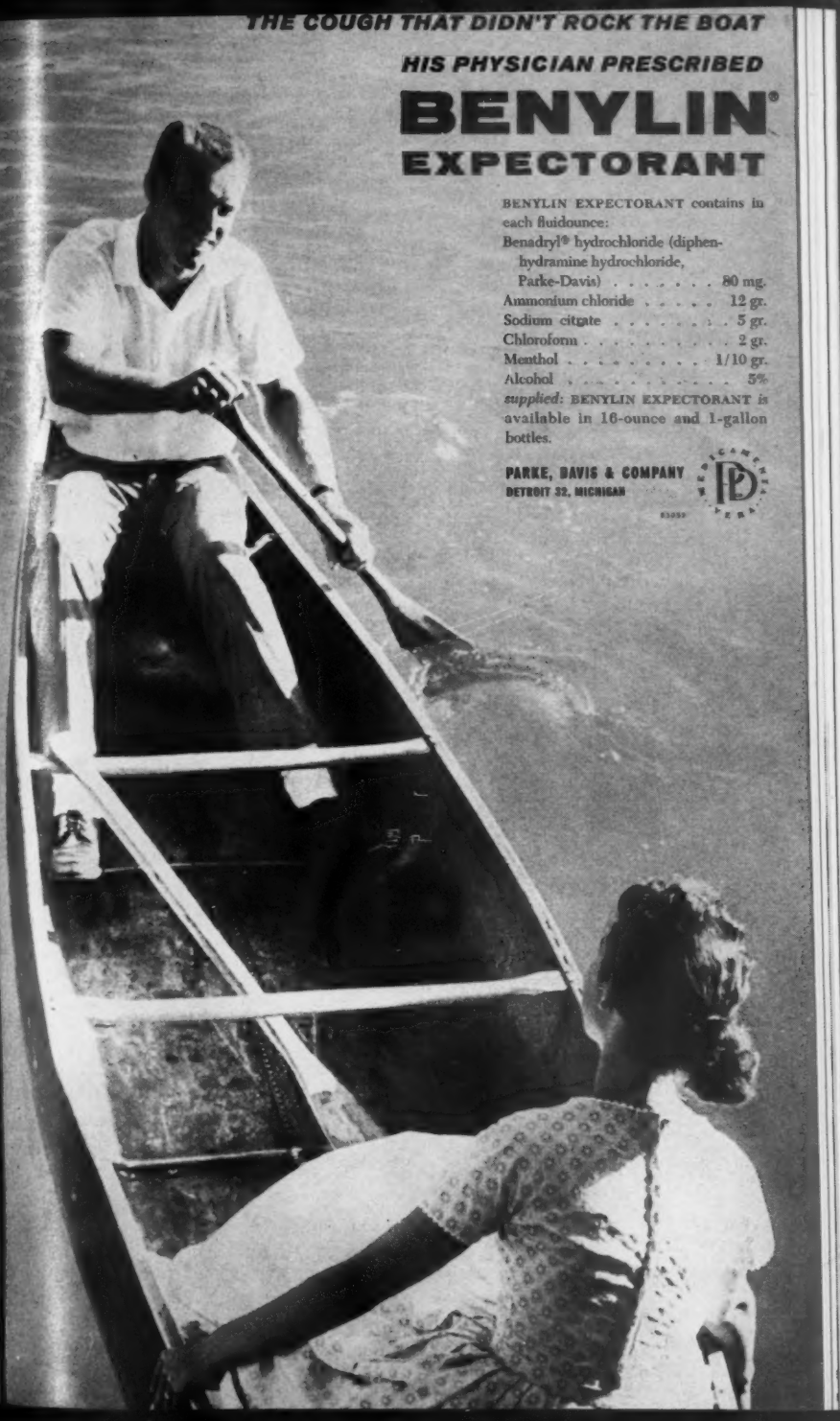
Pack, G. T., *New York J. Med.*, 59:2602-2605,1959.

Steatorrhea

Steatorrhea is the most prominent manifestation in a large group of diseases that might better be termed "small-bowel malabsorptive syndromes." Steatorrhea in the adult is defined as excretion of greater than 5% of ingested fat in the stool. For fat to be absorbed, there must be adequate mixing with bile, and pancreatic and small-bowel enzymes, followed by emulsification into fine droplets, and finally the biochemical change to monoglycerides and free fatty acids.

Steatorrhea may be suspected by the stools rancid odor and its silvery gray or yellow color. The stool fat must be hydrolyzed with glacial acetic acid and heat prior to staining with Sudan III. A study with the patient on a constant amount of fat and collecting all stools may be necessary to detect mild steatorrhea.

In all types some general principles apply. Increasing the dietary fat may increase the fat in the stool, but it al-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so increases the amount of fat absorbed. Adequate protein and carbohydrate are necessary. All vitamins, especially the fat-soluble, should be given orally in water-soluble form and even intramuscularly. Calcium, Vitamin D, iron (intramuscularly), Vitamin B_{12}, Vitamin K, folic acid, electrolytes, and anticholinergic drugs should be used.

Steatorrhea is most commonly seen following subtotal or total gastrectomy, obstructive jaundice, pancreatic insufficiency (usually chronic pancreatitis), lymphoma involving small bowel lymphatics, and non-tropical sprue. Laparotomy is frequently necessary for diagnosis and for treatment. Biopsy of the small bowel mucosa appears to offer the simplest method of differentiating non-tropical sprue from chronic pancreatitis. This biopsy method also has confirmed the diagnosis of Whipple's disease.

Steatorrhea following subtotal or total gastrectomy is poorly understood. The addition of bile salts and/or pancreatin to food, or surgically connecting the hemigastrectomy or esophagus to the duodenum, does not always cure. Obstructive jaundice is almost always a surgical problem. Bile salts in large doses with meals may be used as temporary replacement.

Chronic pancreatitis may exist in all degrees. Substitution is simple, but usually inadequate. Pancreatin, 15 to 25 gms. per day, must be given with meals.

Lymphoma and lymphosarcoma of the small bowel are treated best by the internist and surgeon coordinately, the steatorrhea usually being the minor problem.

Non-tropical sprue is not rare. Mild variants may have existed, asymptomatic, for years until a "flare-up" occurs. Celiac disease in infants and non-tropical sprue in adults are the same disease. The etiology remains unknown. In recent years gluten in the diet has been found to cause exacerbations; its discontinuance has been followed by striking remissions. Steroids have helped in some cases.

A disease which may cause steatorrhea in more than one way is carcinoma of the ampulla of Vater, obstructing both bile salts and pancreatic lipase.

Poliner, I. J., *J. Maine M.A.*, 50:164-165,1959.

Hypertension and Adrenocortical Function

The question of whether and to what extent adrenocortical function is changed in hypertension was studied in 62 patients with a systolic blood pressure of at least 150 mm. Hg. and a diastolic of at least 90 mm. Hg. All but three had essential hypertension. The urinary 17-OH-corticosteroids and 17-ketosteroids were determined following the intravenous infusion of 25 units of ACTH. Patients with fever, edema, hepatic insufficiency, cardiac insufficiency, or pronounced renal insufficiency, as well as those convalescing from infectious diseases or operations, were excluded from the investigation. Most of the patients were on a moderately low-salt diet. Separate evaluations were made for men and for women.

In 40 patients all or some of the tests yielded abnormal results. In cases of "pure" essential hypertension, adrenocortical behavior varied greatly from one individual to another, the values being above or below normal in 40 per cent of the cases.

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Current Concepts in Therapy: Sedative-Hypnotic Drugs II. Chloral Hydrate. New England J. Med. 255: 705 (Oct. 13) 1956

...1 or 2 7½ gr. capsules or 1 or 2 teaspoonfuls of Noctec Solution 15 to 30 minutes before bedtime.

...1 or 2 3¾ gr. capsules or ¼ to 1 teaspoonful of Noctec Solution 15 to 20 minutes before bedtime.

...And 3¾ gr. capsules, bottles of 100. Solution, 7½ gr. per 5 cc. teaspoonful, bottles of 1 pint.

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Both sexes reacted similarly. The severity of the hypertension as reflected by changes in the eye-grounds, left ventricular hypertrophy, or the presence of cerebrovascular lesions, had no demonstrable effect on adrenocortical behavior. Involution of the adrenal cortex due to aging did not appear to be affected by hypertension. When endocrine disorders or autonomic nervous dystonia with anxiety states were present in addition to the hypertension, the results were frequently abnormal.

Quichaud, J., et al., *Presse méd.*, 67:329,1959.

Asthma: Evaluation of Treatment with Theophylline Compounds

A total of 13 asthmatic patients ranging from 23 to 71 years and having had asthma for two to 20 years were alternately given aminophylline 500 mg. I.V., hydroxypropyltheophylline 200 mg. I.V., and an alcohol-water solution of theophylline (Elixophyllin), 2.5 ounces orally to determine the degree to which the drugs would prevent or relieve respiratory depression induced by acetylcholine aerosol. Each patient received a prophylactic and therapeutic test consisting of spirometric function studies of vital capacity and maximal breathing capacity. Epinephrine 0.3 mg. was used as a reference standard in determining improvement. Attacks following administration of the acetylcholine improved to varying degrees following the administration of each drug. Intravenous aminophylline was superior to the other two drugs in elevating the vital and maximal breathing capacities prophylactically, while the aminophylline and the alcohol-water solution were about equal to each other therapeutically. The latter two agents were slightly superior to epinephrine and greatly superior to hydroxypropyltheophylline, both prophylactically and therapeutically.

Frank, D. E., *Antibiot. Med. & Clin. Therap.*, 6:338-342,1959.

Thyroid Cancer in Youth

Of 9 boys and 2 girls with cancer of the thyroid, ages ranged from 5 to 18 years at the time of diagnosis. Persistent enlargement of cervical lymph nodes suggested the diagnosis in 8 of the 11 patients. Total thyroidectomy was the treatment in 7 patients, hemithyroidectomy in 3, and 1 had repeated removal of lymph nodes in the neck, only 1 of which was cancerous. After total ablation of normal thyroid tissue and of as much cancerous tissue as possible surgically, scintigram and/or radioautograph studies with I^{131} in doses of 0.1 to 10 mc., were carried out in 9 of the 11. In 6 of these 9, uptake of the radioactive material was demonstrated. These 6 were treated with I^{131} a dose of 100 mc. being given by mouth. The use of the radioactive agent was continued, with interval studies in which the millicurie doses were used for tracer purposes, only until no further uptake was observed. All through, the patients were kept euthyroid by thyroid hormone or levothyroxine. Follow-up was for periods of 10 months to 9 years. Of the 11, 9 were free of metastases so far as could be determined; 1 had metastatic pulmonary lesions not shown to take up I^{131} and which progressed despite a total dose of 250 mc. of I^{131}. Another had questionable pulmonary metastasis. Nine of the 11 had had x-ray therapy to the head or neck, previous to the diagnosis of thyroid cancer.

Petit, D. W., et al., *California Med.*, 89:394-396, 1958.

Substitution Femoral Head Prosthesis in Primary Treatment of Intracapsular Fracture of the Hip

Many orthopedists have tried the use of a femoral head prosthesis as the *original* treatment of the intracapsular fracture of the hip in order to save an elderly person with a fractured hip spending so many of his remaining days a hip invalid. For patients with a considerable life expectancy it is worthwhile to try for a healed fracture and hope that aseptic necrosis will not develop.

This form of treatment was used in 15 elderly patients. The average age was 79 years, the average hospital stay 15 days postoperatively. All were ambulant to some degree with assistance at the time of dismissal from the hospital.

In all of the 15, an Austin Moore type of intramedullary prosthesis was used. This is a metal prosthesis, cast from Vitallium, with fenestration in the shaft portion through which subsequent bony growth may give further stabilization. At all operations the Minneapolis prosthesis was available, because it is preferable if for any reason the Austin Moore prosthesis is loose in the shaft after insertion. The average operative time, including skin closure, was 70 minutes. About 40% of the 15 received one pint of blood on the table. The anesthesia was spinal block, using six to 10 mg. of pontocaine. Reinforcement has been used to dose any patients who are apprehensive.

Two of the patients succumbed during postoperative convalescence. One, a woman of 85, appeared to tolerate the procedure well and had a good convalescence until the 10th day, when she died of a coronary occlusion. The second, a man of 85, had fallen in a rest home where he was because of age and disorientation. In his convalescence he developed an abrasion, then an open sore on his elbow which flared into a severe cellulitis of the arm uncontrollable with chemotherapy, and he died on the 17th postoperative day. The hip wound had healed well. Another patient had a low-grade phlebitis in both lower extremities. There were no infections in this group. There have been no dislocations of the prosthesis. Postoperatively, no immobilizing apparatus was used. Early motions were encouraged (up in a chair within the first few days, walking with support by the end of the week). Some use the walker, others learn to use crutches. Walking with a prosthesis is much easier since the patient is allowed partial weight-bearing on this leg.

A primary prosthesis does not give as useful a hip as a well healed fracture; it allows early ambulation fa-

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cilitating the care of the very elderly patient; it avoids avascular necrosis in the healed fracture; it allows most patients to be independent in the care of themselves, to be ambulant to the degree required of their years, and may avoid major "hip invalidism" during the waning years.

Carlander, L. W., *Minnesota Med.*, 42:566-570,1959.

Carcinomas of Lip and Tongue

Lesions in these sites are different and must be treated differently. Carcinoma of the lip is confined to the lower lip in over 95% of cases. Provided treatment is undertaken early, good results usually can be obtained either by x-ray, radium, or excision. Suprahyoid dissection may be sufficient for submental nodes palpable at the time of primary treatment. "Prophylactic" dissection of the neck should be withheld until nodes appear. Although carcinoma of the anterior third of the tongue can be treated satisfactorily either by roentgen therapy or surgery, lesions in the middle and posterior thirds of the tongue present discouraging problems. Among 37 cases of carcinoma of the posterior third treated adequately with radiation, 5 year survival was achieved in only 1. Radical excision with concomitant neck dissection gives a salvage rate of 33.3%, with a mortality rate of about 10%. Operation must be early and should include resection of the primary lesion and the neck contents. Prostheses are not necessary. There are 4 contraindications to surgical treatment:

1. A lesion across the midline of the tongue.
2. Fixed nodes in the neck.
3. Draining sinuses in the neck.
4. Evidence of widespread tumor.

Holloway, J. B., *J. Kentucky M.A.*, 56:673,1958.

General Considerations Regarding Acute Reflex Cardiac Arrest

Cardiac arrest, formerly accepted as a happening against which nothing could be done, is now regarded as a condition which must be diagnosed and treated. If occurring during surgery, intervention must be as prompt as possible. Blood pressure readings and ECG are dispensed with. If there is no carotid pulse, the immediate measures are: giving pure oxygen, at first by mask and balloon, and then by intubation; then opening the thorax in the 4th intercostal space, and then opening the pericardium. There then are 2 courses:

1. If no ventricular fibrillation, forceful bimanual massage may suffice, or this may be combined with intracardial injection of 10% calcium gluconate, massage being continued until carotid pulse is felt.

2. If ventricular fibrillation exists, the defibrillator should be used (one should be available in every surgical department). Best results are had with a voltage of 200, with 2.5 to 3.5 amp., and with a shock stimulus lasting at the most 0.1 second. No good will come from defibrillating a heart with deficient oxygen and poor tone.

Myocardial tonicity remaining low after cardiac massage may be raised by injection of 1 mg. epinephrine in 10 cc. isotonic sodium chloride into the left ventricle, or by an intravenous infusion of 40% dextrose.

Hahn, C., & Risch, F., *Helvet. chir. acta*, 25:484-489,1958.

The Anal Papilla

Behind the valves of Morgagni are pockets into which it is possible to introduce a probe to ½ inch, which may be thought of as the seat of infection in this area. These innocent-looking protrusions may be the forerunner of serious trouble. Many anorectal com-

plaints start with a change in the anal papillae and their environs—abscess, fistula, fissure and ulcer, infected hemorrhoids, pruritus ani and pectenosis. The hypertrophied papilla may cause tenesmus, difficult, incomplete stools, or a crawling sensation. A hard stool may pull down the enlarged papilla and tear its base-anal fissure. The papilla stands guard over this tiny tear. Too often fissure, sentinel pile, cryptitis and papillitis occur together.

Bleeding with stool, pain with and after stool, and constipation may be relieved by the use of suppositories giving periods of superficial healing and relief, but the process becomes worse, sometimes with infection of neighboring internal hemorrhoids. Later there are problems as pectenosis, edema and swelling of adjacent hemorrhoids, deeper ulceration with involvement of the external sphincters, beginning fistula and abscess formation, with surgery the only means of cure. The need may be for excision of the sentinel pile and underlying ulcer, the enlarged papilla and the related internal hemorrhoid, and division of the pecten band. Some surgeons incise the external sphincter routinely. This incision usually includes the pecten band. Nestling of the dorsal ulcer or fissure between two hemorrhoids prevents drainage and any attempt at healing. A drop or two of pus may exude from this dorsal site denoting deeper infection before induration has developed. Early excision of an enlarged papilla may abort or limit an infection.

Preventive medicine may progress by the use of the anoscope for examination of the papilla and the adjacent crypts. These problems may be properly appraised and dealt with under saddle-block anesthesia.

Peyton, T. R., *Am. J. Proctology*, 10:206-208,1959.

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Ulcer Therapy with a New Anticholinergic Agent

Oxyphencyclimine (Daricon), a new anticholinergic agent, was clinically evaluated in 80 patients with duodenal ulcer, seven with gastric ulcer, two with jejunal ulcer and seven with hiatus hernia associated with peptic esophagitis. The drug had been administered continuously to seven patients for one year, to 18 for two to six months, to 61 for one to two months, and to 10 for two to four weeks. Usual dosage was 10 mg. given twice daily, usually before breakfast and on retiring. In six patients with severe night pain evening doses were increased to 20 mg. Maintenance dosage in 24 patients following the acute phase of their illness was a single 10 mg. tablet daily.

Satisfactory symptomatic relief was achieved and maintained in 77 of the 80 patients with duodenal ulcer, in all seven with gastric ulcer, in both with jejunal ulcer, and in five of seven with hiatus hernia and associated peptic esophagitis. Radiographic follow-up, done in the seven patients with gastric ulcer and in five with duodenal ulcer, showed complete healing in one patient within two weeks and in the remaining 11 within one month. Side effects included dryness of the mouth, blurring of vision, constipation and urinary hesitancy, and were severe enough in four patients to require discontinuance of therapy. With continued therapy dryness of the mouth often diminished or disappeared.

Winkelstein, A., *Am. J. Gastroenterol.*, 32:66-70, 1959.

Allergic Disorders: Treatment with Dexamethasone

A total of 240 patients ranging in age from two to 70 and presenting in order of frequency bronchial asthma, seasonal hay fever, allergic rhinitis, atopic eczema, allergic conjunctivitis, drug reactions, urticaria, and contact dermatitis, were treated with the synthetic steroid dexamethasone for periods ranging from five days to two months. Most of the patients had already received steroid therapy and were placed on maintenance dosage, while some were started on dexamethasone and later switched to other steroids. Effective daily maintenance dosage for 24 patients when receiving dexamethasone averaged 1.3 mg., compared with 11.6 mg. for 19 when receiving prednisone or prednisolone, 11.2 mg. for 10 when receiving methyl prednisolone, and 9.3 mg. for six when receiving triamcinolone. If both the physician and patient agreed that favorable response outweighed side effects, the results were considered satisfactory. If not, they were considered unsatisfactory. Accordingly 201 patients experienced satisfactory results. Side effects occurred in 72 patients and in order of frequency

included increased appetite with weight gain, nervousness, moon facies, gastrointestinal distress, insomnia, fatigue, depression, muscle pain, and edema. Serious side effects such as peptic ulcer, psychosis, hypertension, diabetes, or osteoporosis were not observed.

Kohn, C. M., & Grater, W. C., *Ann. Allergy*, 17:385-389,1959.

Levophed Favored in Cardiogenic Shock

Prompt infusion of levarterenol (Levophed) to treat shock after acute myocardial infarction significantly is a highly safe procedure and the agent of choice in severe cardiogenic shock. In 55 patients with severe shock after myocardial infarction, and 11 with shock after pulmonary embolism, the mortality rate was 60% in a 1 year period.

With the patients who received arterenol for less than 1 hour before death occurred, the mortality becomes 49%, a marked improvement over the known grave prognosis of cardiogenic shock not treated with vasopressor drugs. Ten of 17 patients treated for shock in less than 1 hour survived. Levophed and digitalis were given to patients in congestive heart failure, with no harmful effects observed. Three of the 55 patients received metaraminol, but blood pressure was adequately maintained in only one, subsequent to relief of shock with Levophed.

A distinct pressor effect was obtained in 42 of the 55 patients with myocardial infarcts, and shock was relieved in 38. Of the 11 patients with pulmonary embolism, a pronounced pressor effect was obtained in 7 and shock was relieved in 5.

Miller, A. J. & Moser, E. A., *J.A.M.A.*, 169:2000, 1959.

Musculoskeletal Disorders: Treatment with a Topical Analgesic

A lubricating analgesic preparation containing organic oils, 30 per cent methylsalicylate and a fat-soluble analgesic agent (Ger-O-Foam) was employed in 41 patients, 30 with chronic and 11 with acute musculoskeletal disorders. Of the 30 with chronic disorders, 6 had osteoarthritis, 5 painful limbs following cerebrovascular accident and hemiplegia, 4 "low back syndrome," 3 rotator-cuff tendonitis, 2 healed fracture, 2 fibromyositis, 2 herniated nucleus pulposis with radiculitis, 2 torn muscle, 1 phantom pain in above-knee stump, 1 rheumatoid arthritis of the lower spine, 1 miscellaneous diseases and 1 pain of unknown origin. Most of the 11 patients with acute disorders had myositis of the trapezius muscle.

Initial treatment involves physical therapy including standard massage, followed by massage with the topical analgesic and exercises where indicated. In three acute cases pain and loss of function was so severe that no treatment preceded use of the topical analgesic. With this regimen complete relief was reported by seven and temporary relief by 15 of 26 patients with chronic disease. All patients with acute disease reported satisfactory subsidence of pain and improvement in function within 2 to 14 days.

These results were corroborated in a blind-test study of four patients selected because of long-standing pain associated with irreversible processes. By reducing pain, the topical analgesic permits administration of a functional exercise program otherwise impossible to follow.

Gordon, E. E., & Haas, A., *Indust. Med. & Surg.*, 28:217-220,1959.

Rapid Poliomyelitis Immunization

In a majority of three groups of subjects, two of adults and one of children, a single inoculation of 10 ml. of poliomyelitis vaccine caused a significantly earlier appearance of neutralizing antibodies than did that of 1 ml. of the vaccine. Within two weeks circulating antibodies to Types 1 and 3 poliovirus were produced by considerably more children and adults given 10 ml. of vaccine than by those given 1 ml., the geometric mean antibody titer in the responding subjects being about 10 times higher after the larger dose. Antibody response to Type 2 poliovirus was rapid and satisfactory with 1 ml. There was no greater discomfort nor any evidence of illness or renal damage following the larger dose.

Baron, S., et al., *New England J. Med.*, 260:966-969, 1959.

Weight Reduction with a New Anorexic Agent

Of two series of overweight patients treated with a new anorexic agent (Levonor), one group of 24 received either the drug or an identical-looking placebo and were placed on a 1,030 calorie per day diet. Of the 12 patients in this group receiving placebos, eight lost less than a pound a week and four gained weight, while the 12 receiving the drug lost an average of 2.5 pounds a week. In the second group 45 overweight men and women ranging in age from 15 to 61 years were placed on a low calorie diet and two or three of the anorexic tablets daily. On this regimen weight loss averaged 2.4 pounds per week. None of the patients complained of insomnia, even when taking the drug as late as 8 or 9 p.m.

Feldman, H. S., *J.M. Soc. New Jersey*, 56:339-342, 1959.

Fatal Sensitization Reaction Following the Use of Pitocin

The use of the oxytocic principle of the posterior pituitary gland (Pitocin) seems to be well-established in obstetrical practice. The risks to mother and fetus have been considered minimal. Though sensitization rarely is a factor in the use of this drug, its use is not entirely free from danger.

A gravida III, para II, aged 30, pregnancy uneventful except for a trace of albumin from the 7th month to term was admitted at term with ruptured membranes. Examination was reported negative, labor spontaneously initiated. An elective induction of labor was attempted by injection of 2 minims of Pitocin *IM*. Within 5 minutes the patient, sitting on a chair chatting with another patient, suddenly became deeply cyanotic, collapsed, and could not be revived.

In all probability the death was due to anaphylactic shock from the oxytocic factor, Pitocin. Clinical investigations suggest that the use of the drug in dilute IV solution is more desirable.

Reports of sensitization to the posterior pituitary hormone are exceedingly rare. Sensitization reactions have occurred only after the drug had been administered on several occasions. In case of history of previous injections elicited, withhold further use of the drug until preliminary skin testing indicates nonsensitization.

A similar precautionary measure might be taken in the use of the ovarian hormone, which has during recent years been administered intrapartum for various obstetrical complications.

Maternal Mortality Study, *Wisconsin M.J.*, 58:314, 1959.

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Severe Respiratory Infection Treated with a Tetracycline Phosphate-Novobiocin Combination

A Negro woman of 40 was admitted to a hospital with a history of anorexia and weight loss for several months. One week prior to admission she became ill with a high fever, cough, ejection of sputum, and later extreme weakness. On admission temperature was 102.6 F., pulse 130 (weak and thready), and she was extremely dyspneic. Chest roentgenogram showed bilateral pneumonia, predominantly of the lower lobes. Repeated sputum examinations for acid-fast bacilli were negative. She was placed on oxygen administered nasally, intravenous fluids reinforced with hydrocortisone and vitamin B-complex, intramuscular penicillin 600,000 units twice daily, and chloramphenicol 250 mg. every six hours. Two days later she was extremely ill and dyspneic, and remained in critical condition despite administration of digitalis, intravenous aminophylline, intramuscular chloramphenicol 1 gm. every six hours, and intravenous erythromycin 500 mg. Sputum showed a staphylococcal and pneumococcal infection, staphylococci predominating. Tetracycline phosphate complex with novobiocin was instituted on the fourth day at a dosage of two capsules every six hours, all other antibiotic therapy being discontinued. Improvement was shown over several days. On the thirteenth day the dosage was reduced to one capsule four times daily, this continued along with multivitamin therapy after her discharge. Two months later, her condition was good and chest x-rays were negative. There were no side effects.

Howell, R., *Antibiotic Med. & Clin. Ther.*, 5:330-331,1958.

Hypercholesterolemia: Effect of Reduced Dietary Fat and Additional Ingestion of Corn Oil

The regimen employed was designed to be acceptable to most patients without radical change in their usual diet and without the use of formula diets. The subjects were nine hospitalized male schizophrenics aged 40 to 55 years, all ambulatory, active and well nourished but not obese. Pretreatment plasma cholesterol levels for these subjects ranged between 247 to 331 mg. Low-fat diet resulted in a mean decrease of 44 mg. per 100 ml. in the plasma cholesterol during the first two months. All subjects lost some weight during this period, the mean loss being eight pounds. With the addition of 90 cc. of corn oil daily to the low-fat diet, cholesterol promptly declined further by 32 mg. per 100 ml. This reduction was fairly well maintained for three months despite an increase in the average weight of the subjects during this period. Return to the routine hospital diet and continuation of corn oil caused an increase of 35 mg. in the mean value for plasma cholesterol. This deviation, about 40 mg. below the control average, was maintained for two months while the corn oil was being taken but returned rapidly to control levels when the use of corn oil was discontinued.

Moderate reduction of saturated fats in the diet and addition of corn oil produce significant lowering of values for plasma cholesterol in humans with hypercholesterolemia. The effect was constant in all nine patients studied but the degree of response was variable. All had a decrease in plasma cholesterol while on the low-fat diet alone.

Rhoads, D. V., & Barker, N. W., *Proc. Staff Met. Mayo Clin.*, 34:225-229,1959.

briefs: DERMATOLOGIC

Dry, Scaling Dermatoses Treated with Tar-Allantoin Lotion

In patients with certain chronic dermatoses, coal tar is useful as an antipruritic, keratolytic and keratoplastic agent for removing crusts and scales as well as minimizing excoriation. Allantoin (glyoxyldiureide) has shown nontoxic healing properties when used topically, or internally in the treatment of gastric and duodenal ulcers. The agent induces healing by stimulating formation of healthy granulations and by removing necrotic material. To test the therapeutic effectiveness of a coal tar-allantoin combination (Alphosyl Lotion) in persistent, chronic scaling dermatologic conditions, 210 patients presenting these conditions were instructed to apply the medication first to a small area, then to all affected areas one to four times daily if no irritation occurred. Actinic ray therapy was administered where indicated and all patients were observed at weekly intervals. Duration of therapy was from less than 2 to 6 months.

Results showed 75 to 100 per cent improvement in 16 of 18 patients with atopic dermatitis, 55 of 68 with chronic infectious eczematoid dermatitis, 9 of 18 with contact dermatitis, 17 of 20 with lichen planus, 20 of 24 with localized neurodermatitis and 55 of 62 with psoriasis. Side reactions to the medication were not noted. Several patients with atopic dermatitis known to react to sunlight when using other tar preparations did not react in the same fashion during therapy with the tar-allantoin lotion.

Welsh, A. L., & Mitchell, E., *Ohio M.J.*, 55:805-807,1959.

Treatment of Antibiotic-Resistant Staphylococcus Skin Infections

Effective measures for treating these cases are:

1. Rigid personal and environmental cleanliness.

Clothing and bed linen should be completely changed daily if possible. Laundering of these articles with sufficient hot water and detergent provides adequate antisepsis. A daily tub bath using a bar soap containing hexachlorophene should be prescribed. After drying with a clean towel the entire skin surface is dabbed with rubbing alcohol or an aqueous solution of 1:3000 bichloride of mercury. When the bearded region is involved, a new razor blade daily and brushless shaving cream containing hexachlorophene help prevent spread of infection. An electric shaver is more traumatizing.

Women should substitute disposable wisps of cotton for powder puffs. The danger of contamination of face creams, rouges, cake type powder and deodorants should be made clear. Nails should be short and scrubbed with a nail brush and hexachlorophene soap three or four times daily.

After a thorough scrubbing, cold cream containing 3% ammoniated mercury is massaged under the nails and on the hands to prevent possible infection from scratching.

Special attention must be paid to bathroom fixtures. Lysol solution should be used on the toilet seat, wash bowl, and tub after use by an infected person.

2. Local use of antiseptic materials.

Solutions for antiseptic washes and packs such as 1:2500-1,3000 aqueous solution of bichloride and 70% alcohol are dabbed on three or four times daily to prevent spread of infection, on an extremity as a wet dressing three or four times daily for one hour. A lotion incorporating antiseptics, e.g.—cinnabar (red mercuric sulfide), 1.0, sulf. precip. 10.0, zinc oxide and talc, 15.0, glycerin, 20.0, 7% alcohol, q.s. ad, 100.0—is applied with an ordinary half-inch flat brush three or four times daily. This is especially useful in hirsute body areas. Another effective lotion applied in the same manner contains resorcin 2.4, burow's solution 15.0, zinc oxide, 30.0, talc 30.0, glycerin, 24.0, calcium water, q.s. ad, 120.0. Ointments containing ammoniated mercury 3-8% and hydrophilic ointment (USP) q.s. ad 30, or sulfur precipitate 3-5%, resorcin 2-4%, and hydrophilic ointment (USP), q.s. ad, 30, are also effective when applied to affected areas two or three times daily.

3. The use of non-specific proteins to increase the patient's resistance.

Although the exact mode of action is unknown, clinical experience has supported the effectiveness of autohemotherapy, 10 cc. at weekly intervals injected deep into the buttocks, and intramuscular injections of boiled milk once or twice weekly, starting with 0.5 cc. and increasing the dose by 0.5 cc. increments once or twice weekly until a maximum dose of 5 cc. is reached.

4. Attempts to increase resistance by vaccines and bacterial products.

An autogenous vaccine may be made but practically the same results are obtainable by the use of staphylococcus toxoid in ascending doses. An intradermal test is made initially, with 0.05 cc. of the toxoid. Occasionally marked sensitivity is shown to this dose, requiring dilution of the toxoid by 10 times for the initial treatment dose. When the proper initial dose has been determined successive weekly doses are increased by 0.05 cc. until 1 cc. is reached. The doses may be given either intradermally or subcutaneously. When the larger doses are reached it is necessary to change to the subcutaneous route.

5. Fractional x-ray therapy to localized area of recurrent infection.

In most cases 75 r can be given at weekly intervals from four to six times with good results. When given with care there is no fear of any x-ray sequelae.

Swarts, W. B., *Connecticut Med.*, 22:820-921,1959.

briefs: PEDIATRIC

Hand-Schuller-Christian Disease: Case with Multiple Bone Defects

An infant of 20 months had for the last 6 months been suffering irregular fever and had lost much weight. On the scapular and cranial bones, tumors had appeared one after the other. Apparently pain was felt in all bones. The tumors were gelatinous and did not respond to treatment with streptomycin and isoniazid. X-ray examination showed osteolytic lesions, only the bones of the hands and of the feet being spared. Other findings were grave hypochromic anemia, hypercholesteremia, high leukocyte count with pathological granulations of the neutrophils. The patient was given liver extract, vitamin compound, iron, a normal diet with some limitation of cholesterol, and x-ray therapy, 100 *r* over each focus to a total dosage of 300 to 500 *r*. Generally, one series induced recalcification, but some of the lesions required a 2nd series, which was given 4 to 7 months after the first. After 3 months great improvement was shown, the blood became normal, the osteolytic lesions, one after another, became calcified in the course of 2½ years. The patient was discharged as cured, and 2 years thereafter cure was shown to have been well sustained.

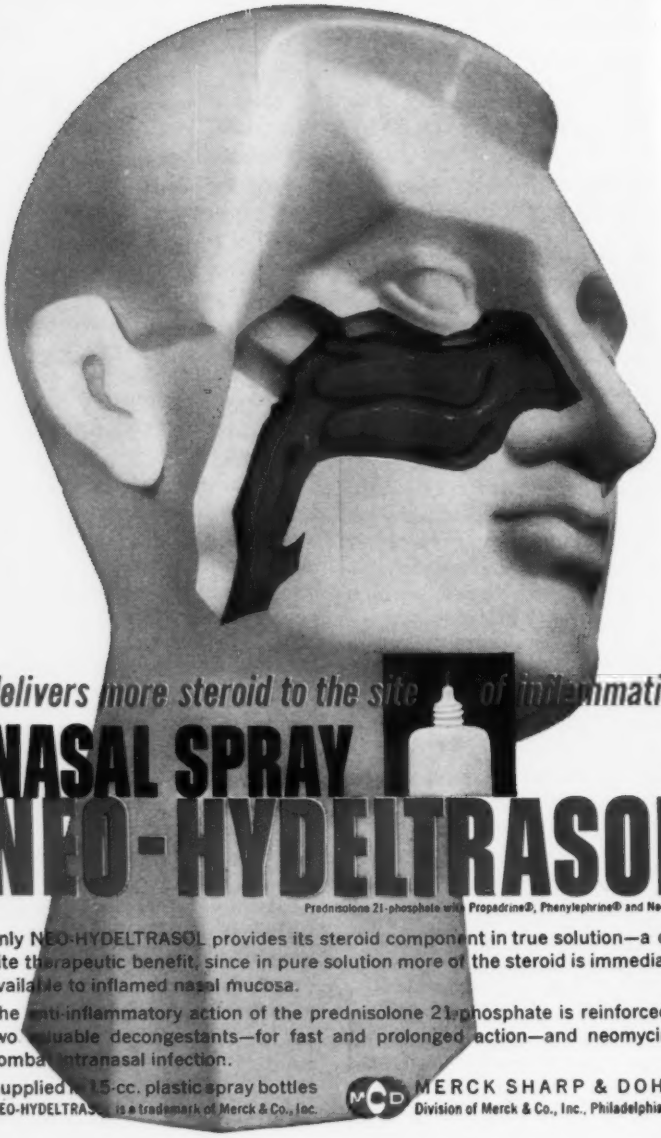
Niclos, M., et al., *Rev. españ. pediat.*, 14:763-782, 1958.

Acute Epiglottitis: A Childhood Emergency

Of 42 children sent to the hospital with this infection referring diagnosis was accurate in only one, yet 3 who died on the way and 2 others who died shortly after admission had been ill less than 6 hours. Of the remaining 37—all of whom were saved—17 had been ill less than 8 hours and only 1 for 24 hours.

The syndrome is characterized by abrupt onset of extreme throat pain, difficult breathing, marked dysphagia, excessive drooling and progressive restlessness. It is most common before 8 years of age. Of the 42 children, only 1 was more than 8 years old and only 11 were less than 2. Though accumulation of oropharyngeal secretions (due to difficult swallowing) is usual, signs of pharyngitis seldom are striking. Neither fever nor respiratory rate seems related to toxicity or extent of respiratory obstruction. Unless treated, the course usually is rapidly disastrous, with progressive respiratory obstruction, shock and death. Haemophilus influenzae, Group B, is the most common causative organism.

Beside diagnosis is not difficult. The cherry-red, swollen epiglottis obstructing the pharynx is unmistakable. Depression of the tongue during throat inspection is mandatory. These children should be hospital-



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ized. They need constant nursing care, frequent medical surveillance, and cool, humidified air. Tracheotomy is the cornerstone of conservative management, and must be performed without delay as soon as indicated. All of 18 children saved despite the fulminating course of their illness were tracheotomized. Early tracheotomy almost certainly would have saved the 5 who died. Specific therapy currently used is chloramphenicol I.M. in doses of 100 mg./kg. for the first 24-36 hours, and 50 mg./kg. orally thereafter if tolerated.

Berenberg, W., & Kevy, S., *New England J. Med.*, 258:870-874,1958.

Threat of Neonatal Asphyxia in Bilateral Bony Atresia of Posterior Nares

Choanal atresia in the newborn, when bilateral, is a surgical emergency. Unable to breathe at all through the nose, these infants also have extreme difficulty in mouth breathing — apparently because uncontrolled movements of the tongue and soft palate obstruct the airway. With intermittent success in getting a little air, they become critically dyspneic. Even when able to achieve enough mouth breathing to prevent asphyxia, they are in danger of death by starvation because of difficulty in sucking or swallowing and breathing at the same time. Experience with early surgical treatment in 3 cases prompts the following recommendations:

1. For immediate relief, insert small airway (oral type used in anesthesia) to hold mouth open, with tongue down and forward. Then provide uninterrupted supervision of breathing.

2. Treat surgically, as soon as possible, by penetration of choanal obstructions.

3. Pass polyethylene tubes from nares into pharynx just below margin of soft palate, suturing these to tracheostomy tape held across upper lip by adhesive tape on cheeks. Teach parents to suction and clean tubes.

4. Dilate choanae at intervals of 2-3 weeks.

5. As infant grows, fit new breathing tubes, using standard endotracheal anesthesia tubes cut to length. Remove when indicated, replacing intermittently to keep choanae open.

Of 3 infants treated successfully by operations on the 1st, 3rd, and 16th days of life, dilations were continued for 20 months in the one followed longest. Though x-ray studies at 23 months showed that 1 choana had reclosed, the child still appears healthy at 3 years of age.

Morrow, R. C., *J. Maine M.A.*, 49:135-136,147,1958.

Staphylococcal Pneumonia in an Infant: Treatment with Nitrofurans

The nitrofurans have been shown to be highly effective against staphylococcal strains resistant to other antibacterial agents, possessing the additional advantage of limited and slowly acquired bacterial resistance. In a boy of four months, successful treatment of diagnosed staphylococcal pneumonia was achieved with nitrofuran therapy after resistence had been demonstrated against penicillin and allergy shown to chloramphenicol.

The child was hospitalized with a three weeks' history of mild upper respiratory infection, the main symptoms being cough, fussiness, and transient elevations in temperature. On admission he was placed in a croup tent with cold steam oxygen and mucolytic detergent solution, and given 300,000 units of aqueous penicillin every four hours. There was little change for 36 hours except that rectal temperature rose to 103°F. On the third day, chest x-ray revealed fluid within the pleural space and in the right interlobar septum, and the child began to develop a productive cough. Sputum was obtained for smear and culture, both of which revealed Staphylococcus aureus, sensitive only to chloramphenicol, bacitracin and nitrofurantoin (Furadantin). Chloramphenicol was administered I.M. in 100 mg. doses every 6 hours, following the third dose of which the child became increasingly irritable and developed a generalized urticarial eruption.

In view of the apparent allergy to chloramphenicol, nitrofurazone solution was instilled intrapheurally, the commercially available 0.2 per cent solution being diluted with an equal amount of sterile physiologic saline and 10 cc. of this mixture instilled twice daily. The appearance of the fluid draining from the pleural space changed almost immediately, becoming thinner and less tenacious. Within 24 hours after irrigation was instituted the child became less irritable and voluntarily resumed taking of food. Instillation of nitrofurazone was then discontinued and nitrofurantoin oral suspension administered, 4 cc. every four hours. Within another 24 hours the child was afebrile, and chest x-ray showed marked diminution of pleural fluid and almost complete re-expansion of the affected lung. Recovery was uneventful and without sequelae.

Perkins, J. L., & Openshaw, C. R., *J. Kansas M. Soc.*, 60:250-252,1959.

Treatment of Whooping Cough in Nurslings and Small Children

Among nurslings and children under 5 years with whooping cough, 1621 were treated between 1941 and 1957. Of this number, 1051 (group I) were treated between 1941 and 1946, 286 (group II) between 1950 and 1952, and 284 (group III) between 1955 and 1957. Of those in group 1, 109 died (10.38%); of those in group II, 11 died (3.84%); of those in group III, 4 died (1.40%). This great improvement is attributed to use of antibiotics (such as chloramphenicol and streptomycin) and hyperimmunized human gammaglobulins, use of active sedatives, and nursing adapted to the needs of the patient, including use of an aspirator, maintenance of correct aeration, oxygen after severe paroxysms, and full feeding by small, frequent meals.

Marie, J., et al., *Rev. immunol.*, 22:432-455,1958.

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May) 1958. Haycock, C. E.; Davis, W. A., and Morton, T. V.: Am. J. Surg. 97:75-78 (Jan.) 1959. Stone, M. L.; Schlussel, S.; Silbe
Feb.) 1956. Schulte, F.: Deutsche med. Wchnschr. 80:1188-1191, 1957. Frazer, W. A.; Flowe, B. H., and Anlyan, W. G.: J.A.M.A.

Infections in Children Treated with Glucosamine-Potentiated Tetracycline

A group of children ranging from one month to 14 years was given glucosamine-potentiated tetracycline in various oral forms for the treatment of tonsillitis, bronchitis, pharyngitis, bronchopneumonia, otitis media, various upper respiratory infections, gastroenteritis, encephalitis, boils, gingivostomatitis, roseola, abscess, cellulitis, and pyelitis. Medication was administered as capsule, oral suspension, or drop, on an average daily divided dosage of 25 mg./kg. body weight. Regimen was continued for at least 3 days after the patient became afebrile. Within 72 hours 80 children became afebrile and all responded to therapy within 10 days. Side effects, including gastrointestinal upset and diarrhea, were absent in all cases. In some instances the medication proved superior to penicillin, erythromycin, or other antibiotics.

Mathieu, P. L., Jr., et al., *Rhode Island M.J.*, 42: 172-174,1959.

Use of a Nasal Antibiotic Cream in Staphylococcal Disease

During the fall of 1957 public-health nurses in a central New York community noted a number of pustular skin lesions in newborn infants after discharge from a hospital in the area. This information was communicated to the local health officer during the first week in December. Of 97 infants delivered during October and November, information was available on 59. Significant skin lesions consisting of bullae, pustules or abscesses were evident in 19 (32%) of the infants.

The nurses see 60% of the infants born at the suspect hospital, usually within two weeks after discharge. A sampling of lesions of infants seen during the first week of December was cultured and phage typed. Nasal cultures were taken from nurses and doctors, since no lesions were apparent among hospital personnel at this time. Cultures demonstrated a coagulase-positive hemolytic staphylococcus, Type 80/81, in the lesions of two or three infants and in the nasal cultures of two nurses and two physicians.

During the first week in December the nursery was closed to all new admissions and a second nursery was opened. After all newborn infants had been discharged from the initial nursery, it was cleaned and placed back in operation. During February, an increase in the number of lesions was evident. Of six neonatal lesions cultured during February, all were Type 80/81. The nursing personnel were cultured. Once more, a careful check of technic used in the nursery was made, and a new nursery was set up. The nasal ointment—2.5 mg. of neomycin and 0.25 mg. of gramicidin in a bland base—was applied four times a day to the anterior nares for one week. All nurses having any contact with the nursery were treated. All newborn infants in the nursery or entering the nursery during this period were treated until discharge.

During the six months before March, 29% of the newborn infants had a significant skin lesion. This dropped to 12% in March and to zero during the succeeding four months.

The use of nasal creams in outbreaks of nursery staphylococcal infections that resist other methods of control deserves further study.

Klein, J. O., & Rogers, E. F. H., *New England J. Med.*, 260:1012-1015,1959.

Serous Otitis Media as an Allergy in Children

Chronic middle ear disease in children can be managed best when the probability of allergy as a factor is recognized. Results in approximately 200 cases justify the conclusion that serous otitis media, when accompanied by a nasal smear positive for eosinophils and by positive skin tests, can be regarded as allergic in origin and therefore amenable to allergic treatment. In a series of children referred with the presumption of allergy, allergic management was successful for all but 1 of 16 found definitely allergic, but was unsatisfactory for all of 14 whose nasal smears were negative and whose skin tests were negative to mildly positive.

Infection associated with the allergy should be controlled simultaneously. Some infections resistant to all other therapy, including surgery and radiation of the nasopharynx, responded satisfactorily to treatment with injections of gamma globulin (0.1 cc./lb. body weight every 4-6 weeks) combined with allergic management. In some cases, even though allergy was definitely diagnosed, allergic treatment had to be supplemented by control of lymphoid hyperplasia (by surgery or irradiation or both).

Solow, I. A., *Ann. Allergy*, 16:297-299,1958.

Perinatal Mortality

Vasa previa, placenta previa, placenta previa Cesarea, abruptio placenta and occult placental hemorrhage from a fetal circulatory defect are the usual precursors of post hemorrhagic shock of the newborn infant. There must be many degrees or gradations of hematogenic shock in the newborn. It is suggested that the symptom-complex "hyaline membrane disease"—dyspnea, cyanosis, labored respirations with sternal retraction and tachypnea—is basically the hematogenic shock syndrome and that hyaline membrane is a secondary or incidental finding. Infants of diabetic mothers, in whom hyaline membrane disease has a high incidence, do not fit into this category.

Extreme degrees of this condition are recognizable at birth by the dyspnea, tachypnea and cyanosis. Their respiratory rate increases steadily, they go downhill rapidly and they die, presumably from exhaustion. In lesser degrees symptoms appear to in four hours later and follow the same basic pattern. There is usually a history of early separation of the infant from its placental blood supply. After a symptom-free interval, apnea, cyanosis, tachypnea and dyspnea with grunting labored respirations are manifested.

The birth history and the history of the onset of symptoms are useful guides for deciding whether or not a transfusion is indicated. Hemoglobin determinations and red blood cell counts are often of no help in deciding upon transfusion as treatment. There is no evidence that the transfusions were harmful to any of the infants treated. It is suggested that blood transfusions be given in those instances in which history and findings indicate that the newborn infant has lost blood. They serve as prophylaxis and treatment of abnormal pulmonary ventilation, especially in those infants who have been deprived of their placental blood.

Landau, D. B., *Missouri Med.*, 56:530-538,1959.

briefs: GYNECOLOGIC

Spontaneous Healing of Large Rectovaginal Fistula

Rectovaginal fistula is now a rarity. Some of these fistulas require no treatment. The inconveniences they produce when gases and liquid stools escape are accepted. Large fistulas in the roof of the vagina, allowing a good deal of feces to enter the vagina demand treatment. The chief hindrances to closure—spontaneous or surgical—are infection, poor blood supply, and tension on healing tissues.

A woman of 47, para O, gravida O, weight 235 lbs. complained of abdominal enlargement and menstrual pain—felt for many years, and increased for past six months. For 10 years she had had increasing abdominal discomfort with periods, for less than a year severe enough to send her to bed. The uterus was irregularly enlarged to the size of a 4-month gestation, firmly fixed in the pelvis and painful on manipulation. The lateral fornices and posterior cul-de-sac were foreshortened, full, tense and tender. The recto-vaginal septum and uterosacral ligaments felt thickened and tender.

At laparotomy a multinodular fibroid presented with adhesions to everything in the pelvis, especially marked about the ovaries, posterior surface of the uterus and the recto-vaginal septum. With no apparent injury to the surrounding structures, total hysterectomy and double salpingo-oophorectomy were finally concluded.

All went well until the 5th day when nausea, vomiting and diarrhea began. By the end of the 6th day, under medications, nausea and vomiting had stopped and constipation had supplanted the diarrhea. Slow seepage of liquid feces began from the vagina on the 7th day. The enema given on the 8th day returned through the vagina. The proctologist believed that self-closure of the 3-cm. fistula would occur under intestinal antisepsis by aureomycin at first and sulfathalidine later, both in full dosage; and control of diet and flatulence, semisolid stools and encouragement of granulation by gentle packing from the vaginal side after insufflation with powdered aureomycin daily for the first two weeks. After several days of progress a standstill or even regression was observed. At the 6th week the fistula was about to close. Home on the 15th day, the

he'll be under way again soon, once he's on

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patient received all subsequent care in the office. Everything that was tried to mask the horrible odor failed. At the suggestion of an enterprising housewife, the burning of ground coffee was tried and fortunately it worked. When the fumes from the burning coffee cleared away, the room was free of all disagreeable odors

Bell, H. G., *Am. J. Proctology*, 10:139-143,1959.

The Early Detection of Uterine Cancer by Use of the Papanicolaou Smear

A total of 1237 patients studied over a period of 18 months ending in December of 1957, showed as follows:

Group 1. Negative	903
Group 2. Hyperkeratosis; trichomonas; atypical cells—negative Metaplasia—negative	234
Group 3. Atypicality—repeat smear recommended	37
Group 4. Atypical cells—biopsy recommended	23
Group 5. Suspicious—conization recommended	18
Group 6. Positive smears—conization recommended	22
	1237

Uterine cancer can be detected earlier by the cervical (Papanicolaou) smear than by any other method presently known. Some 25,000 women die each year from uterine cancer. The need for the Papanicolaou smear as an integral part of the examination of every woman is obvious. The time required to obtain such smears is less than one minute per patient.

The cervical smear is a screening device and does not afford a diagnosis. All abnormal smears must be confirmed by appropriate tissue study.

Long, R. C., *J. Kentucky M.A.*, 57:690-692,1959

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briefs: OPHTHALMOLOGIC

Eye Signs in Head Injury

Eye signs are important gauges of the severity of head injuries and of the need for neurosurgical consultation. The following are helpful in prognosis and differential diagnosis:

1. Inability to close eye: Facial nerve injury, peripheral or nuclear.

2. Complete ptosis of an eyelid: Third nerve injury.

3. "Black eye": Fracture of base of skull if hemorrhages in lids are limited to orbital margins. Lid discoloration shows first in midlower lid, hemorrhage on eyeball does not move, conjunctiva is not red at first but becomes purplish in several days, and there is as much blood as edema.

4. Dilatation of pupil: Brain swelling with herniation of hippocampal gyrus of temporal lobe, if there is no ptosis early.

5. Loss of corneal reflex: Injury involving ophthalmic branch of fifth nerve, its central connection, or facial nerve or its nucleus.

6. Conjugate deviation: Injury of brain (site uncertain).

7. Paralysis of ocular muscles: Lesion at apex of orbit or subarachnoid hemorrhage at base of brain.

8. Nystagmus: Involvement of labyrinth or connections of vestibular nerve.

9. Papilledema: Edema of brain, if blindspots continue to enlarge 12 hours after injury.

10. Exophthalmos with pulsation and bruit: Arteriovenous fistula in cavernous sinus, from injury to side of head or lateral wall of orbit.

Because the facial nerve has been damaged in 20% of reported cases, it is essential to remember that with this injury the cornea must be protected. For diagnosis of papilledema, a detailed record of changes in the fundus is needed. Tests of vision have medicolegal as well as clinical value and should be given when feasible. The dilated pupil, a sign of herniation of the temporal lobe, is a warning that sight in the affected eye, and life itself, may be threatened.

Harms, H. H., *J. Louisiana M. Soc.*, 110:127-133, 1958.

Prevention of Toxemias and Other Complications of Pregnancy: Contributions of Ophthalmology

The need for cooperation between obstetrician and ophthalmologist is clearly demonstrable in the toxemias of pregnancy. Paramount in their management is early recognition. Routine ophthalmoscopy is necessary since the vascular changes characteristic of the progress of the toxemia are readily apparent in the retina. The first sign of impending circulatory difficulty is narrowing of the re-

tinal arterioles. The second stage is marked by localized spasm of arterioles and of the temporal arteries near the disk. This finding in a diabetic patient usually indicates death of the fetus. The third stage is the typical toxemic retinopathy (ischemia, edema, hemorrhage and transudation), which signifies permanent vascular changes. This retinopathy, if seen prior to the 28th week of pregnancy, means there is only a 25% chance of a live baby and almost no chance that the mother will escape permanent circulatory damage. Ocular signs to be regarded as indications for terminating pregnancy include:

1. Toxemic retinopathy.

2. Detachment of retina as result of toxemic intra-ocular edema.

3. Retinal hemorrhage, transudate or papilledema associated with hypertension.

4. Retinal hemorrhage during pernicious vomiting.

5. Retinopathy associated with severe eclampsia and diabetes.

A number of congenital ocular defects are attributable to minor febrile illness during the first trimester. Anophthalmia, microphthalmus and congenital cystic eye are the most likely if the illness is in the first month. If in the second, congential cataract and disturbances of retinal differentiation are more likely. Therapeutic abortion should be considered if rubella is contracted during this trimester. For young women not having had the disease in childhood, deliberate exposure before pregnancy is recommended. A valuable contribution to the study of congenital defects could be made if during pregnancy women were encouraged to keep accurate daily health records to be correlated with examinations of their newborn.

Givner, I., *West Virginia M.J.*, 54:65-69, 1958.

Treatment of Conjunctivitis

The most frequent cause of bacterial conjunctivitis in the newborn is obstruction of the lacrimal duct, followed by dacryocystitis. This can usually be eliminated with two probings, while the conjunctivitis responds promptly to sulfonamide drops or ointment. Blepharoconjunctivitis in children of school age is often due to visual disorders and corrected by prescribing glasses. To accelerate recovery, eye drops containing 0.1 per cent zinc sulfate and 0.1 per cent Privine as recommended. In vernal conjunctivitis, these drops combined with an anaesthetic, local treatment with hydrocortisone or prednisolone, and in certain cases concomitant oral administration of prednisone are beneficial.

Bacterial conjunctivitis in adults is treated in the acute stage with broad-spectrum antibiotics combined with Ultracortenol or hydrocortisone eye drops instilled every two hours. Despite this treatment, the disease may persist for weeks or months, and relapses are not infrequent if the corticosteroids are discontinued too soon. Satisfactory results have often been obtained in severe cases of Sjogren's syndrome by closing the lacrimal duct with the aid of diathermy. Perandren, iron preparations, and vitamins of the B complex are indicated as general measures.

Franceschetti, A., *Méd. et hyg.*, 17:56,1959.

Doctors and the Law

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CHARLES J. FRANKEL, M.D., LL.B., *Editor*

►Can the board of a private hospital withdraw a doctor's staff privileges, without any charges of misconduct having been made, where the bylaws of the staff provide for procedural rules for government of staff members?◄

This question was before the Supreme Court of Suffolk County, New York, in 1959 (*Manczur* vs *Southside Hospital*, 183 N.Y.S. (2d) 960). Plaintiff doctor had been appointed to the hospital's "courtesy staff" annually since 1952. In August, 1956, the hospital director notified him his obstetrical privileges had been withdrawn. The action was taken without any recommendation by the medical staff and plaintiff was not subsequently reappointed. No charges of misconduct had been made against him and plaintiff was not afforded an opportunity to present any defense against the withdrawal of the privileges.

The Court said that in the case of private institutions, absent of any contractual relationship or agreement to the contrary, the exclusion of a doctor from staff privileges is a matter entirely within the discretion of the managing authorities. Plaintiff contended that here there was a contract which limited the hospital's authority to exclude doctors from staff privileges. He argued that the staff bylaws, because they were approved in the hospital's constitution and bylaws, constituted a contract between

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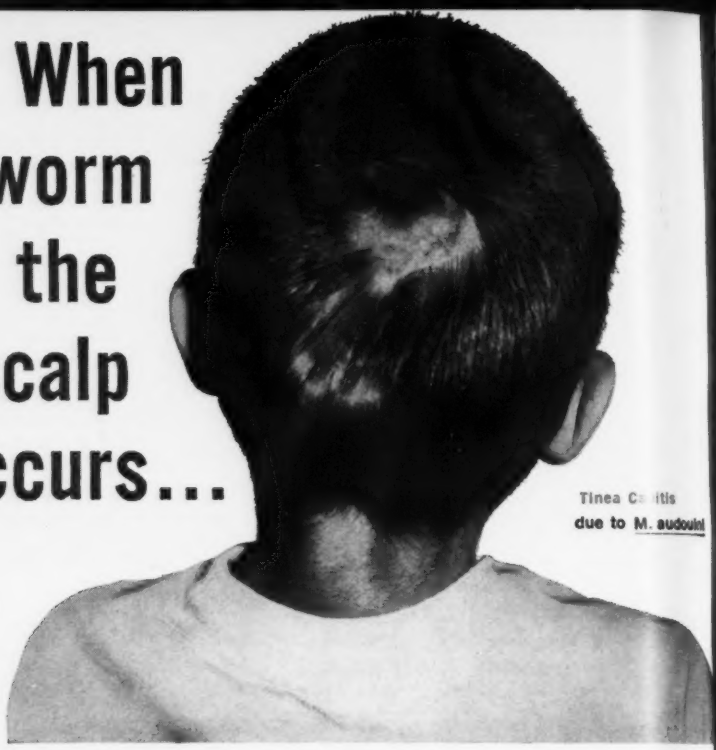

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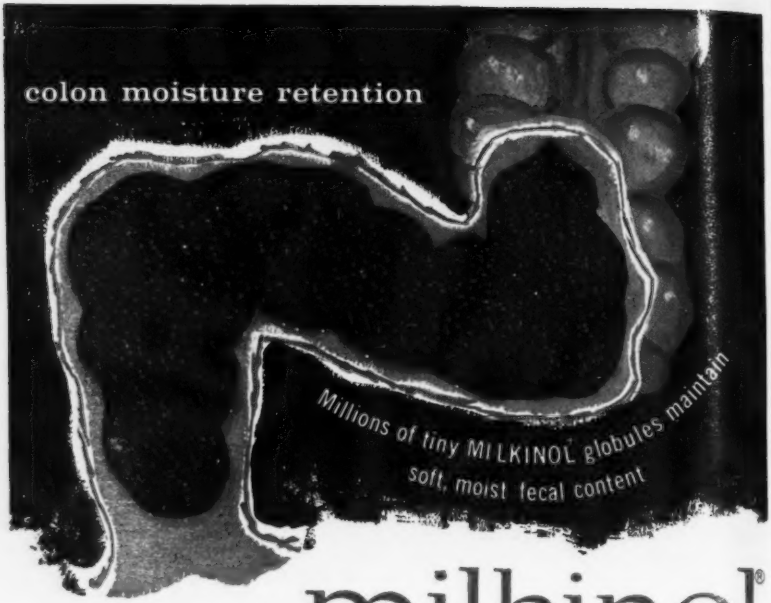
the hospital and members of the medical staff. The staff bylaws set forth a strict procedure for the removal of any member of the staff by its own governing body, known as the medical board, on its own initiative or on charges preferred by the hospital board. Plaintiff contended that failure to follow this procedure constituted breach of contract.

The Court said the staff bylaws may provide procedural rules for the government of staff members in their own association, but it is not a contract between the staff and the hospital, and the hospital board is not obligated to follow the procedures provided therein. The hospital's constitution provides generally that the medical board shall "define the duties and privileges" of staff members, but does not obligate the hospital to follow the procedures designed for the staff's self government. In its own bylaws, the hospital reserves to itself the right to conduct its own affairs. Further, the provision of the staff bylaws, which sets forth the procedure for a staff member's removal, provides that nothing therein "shall be deemed to limit or restrict the power . . . of the governing body of the hospital to maintain control and administer the hospital and its staff . . .". The staff bylaws and the hospital's constitution taken together spell out no mutuality of obligation requiring the hospital to follow a procedure set by the medical staff for disciplining its members. The withdrawal of plaintiff's staff privileges was, therefore, lawful.

▶Is the doctrine of res ipsa loquitur applicable in a case involving injuries which developed following an injection of Pentathol Sodium?◀

The Supreme Court of California passed on this question in 1959 (*Wolfsmith* vs *Marsh*, 337 P. (2d) 70). Plaintiff was hospitalized for the purpose of determining the cause of her obesity. She was nervous and in somewhat poor health, but suffered no particular pain or discomfort. Plaintiff underwent various tests and examinations and her doctor finally ordered that she be given basal metabolism tests. Because of her nervous condition and emotional makeup, he ordered one such test to be given under Pentathol Sodium and another without it. After his attempts to inject plaintiff's left arm were unsuccessful, defendant injected the inner aspect of her right knee. When plaintiff was returned to her room, she complained of excruciating pain in her leg. Within a few days after the injection, a thrombosis developed, and shortly thereafter a "slough ulcer" appeared at the site of the injection. Plaintiff remained in the hospital more than two months during which time she suffered constant pain in her leg. When the pain continued after her release from the hospital, plaintiff consulted another doctor, who upon examination of her leg, found a scar into which ran two visible varicose veins. He concluded she had phlebitis, anterior tibial strain due to the manner in which she walked to ease the pain and that at the point of the injection she was suffering from causalgia. The vein, which was diagnosed as varicose, was removed from the groin to the ankle and the scar on her knee was removed by surgery.

Plaintiff contended the jury should have been instructed that the doctrine of res ipsa loquitur was applicable. In order for the doctrine to be applicable the following conditions



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must be met: (1) the accident must be of a kind that ordinarily does not occur in the absence of someone's negligence; (2) it must be caused by an agency or instrumentality within defendant's exclusive control; and (3) it must not have been due to any voluntary action on plaintiff's part. It was conceded that the last two conditions had been met. In determining whether the first condition has been met, courts have relied upon both common knowledge and the testimony of expert witnesses. The Court said that it is a matter of common knowledge that injections in the body do not ordinarily cause trouble unless unskillfully done or unless there is something wrong with the substance injected. There was also expert testimony that the injection of Pentathol Sodium into a varicose vein would not be in accordance with the standards of medical practice in the community and that plaintiff's difficulties were the result of such an injection. The jury should, therefore, have been instructed on the doctrine of *res ipsa loquitur*.

►May a court transfer custody of a 14 year old boy from his parents to Commissioner of Social Welfare for purpose of getting consent to surgery on the boy?◄

The New York Court of Appeals passed on this question in 1955 (*In re Seiferth*, 127 N.E.(2d) 829). The boy had a harelip and a cleft palate. His father refused to allow surgery because of his belief in mental healing by letting "the forces of the universe work on the body." The father had inculcated a distrust and dread of surgery in the boy since childhood. The boy opposed the operation even after receiving a full explanation of the surgical procedures involved, being shown photographs of results of similar remedial surgery on other children and hearing comparisons of his speech with that of children who had undergone the remedial surgery.

A plastic surgeon testified as to the surgical procedures involved and stated that the only risk of mortality is the one due to the use of anesthesia. He stated there was no emergency requiring immediate performance of the operation but that the earlier surgery is performed, the better the results. After the operation, the boy would be able to talk normally only after going to a school for an extended period for concentrated speech therapy.

The Court said that the Children's Court has power in drastic situations to direct an operation on a child over its parents' objections. Here there is no present emergency. Further, in order for the boy to benefit from the surgery, it would be necessary to get his co-operation in developing normal speech patterns through a long course in concentrated speech therapy. It would be almost impossible to get his co-operation if he continues to believe, as he now does, that it will be necessary "to remedy the surgeon's distortion first and then go back to the primary task of healing the body". The Court concluded that less would be lost by permitting the lapse of several more years, when the boy may make his own decision to submit to plastic surgery, than might be sacrificed by compelling him to undergo it now against his sincere and frightened antagonism.

►Can a corporation, engaged in selling prepaid medical and hospital plans and in providing the medical, surgical and

hospital services required by the plans, deduct from its gross income, as an ordinary and necessary business expanse, payments to its stockholder doctors in excess of 100% of the base fees billed by the doctors?◀

The U.S. Court of Appeals, 9th Circuit, passed on this question in *Klamath Medical Service Bureau* vs *Commissioner of Internal Revenue*, 261 F.(2d) 842 (1958). The corporation's principal business is selling prepaid medical, surgical and hospital plans in Klamath County, Oregon, and providing the services required under the plans. Its primary source of income is premiums paid on the plans; it receives some additional income from noncontract patients using the hospital facilities it owns. Stock ownership is limited to members of the Klamath County Medical Association. To provide the services required by the plans, the corporation entered into contracts with all members of the county medical association, whereby they agreed to furnish the necessary services and to a schedule of base fees for each service performed. When a doctor bills the corporation for a service rendered, he is paid 50% of the base fee within thirty days. Then every six months the corporation pays him (less the 50% already paid) a percentage of the base fees billed by the doctor, determined by the ratio which the corporation's total net income (less certain amounts determined by the board to be necessary for corporate purposes) bears to the total fees billed by all the doctors during that six month period. In short, the corporation determines what its net profit will be, deducts amounts necessary for corporate purposes, and then pays out a percentage of its profits to the doctors, regardless of what the fee schedule amount would be since the latter is only a *base* fee. During the years in question payments to the doctors amounted to 116.9, 115.7 and 134.3 per cent of their billings.

The corporation contended the Tax Court erred in its finding that the payments in excess of 100% of the doctors' base fee billings were distributions of corporate profits rather than compensation for services. It argued that, in determining whether contingent payments, such as are involved here, are to be regarded as distribution of profits or as compensation for services, the following factors are to be taken into consideration: (1) Do the payments bear any relation to the stockholdings? (Here, the answer is no, because each doctor has one share, but each is paid on the basis of services performed); (2) Are the payments in proportion to services performed? (Here, that fact is undenied); and (3) Are the payments reasonable in amount? (The Tax Court held they were reasonable up to 100%, and indicated that it felt they were reasonable as to the amounts actually paid). Since all of these questions were properly answered, it is the contention of the corporation that the amounts paid in excess of 100% of billings should be deductible as compensation for services, an ordinary and necessary business expense.

The Court said there was sufficient evidence to support the Tax Court's holding that the payments in excess of 100% of billings were a guise for distributing corporate profits. The Court further pointed out that the corporation's contracts with the doctors obligated it to pay them 100% of the base fee, however and at what-

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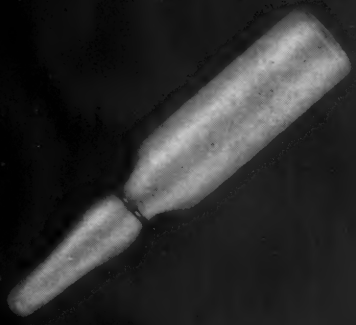

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ever figure it was set, but no more. Any amount over and beyond the 100% base fee could, or could not, be paid to the doctor-members as the management saw fit. The voluntary payments to the doctors of more than the 100% of the base pay they had contractually agreed to accept as full payment for their services, might be an ordinary, but could not be a necessary, expense and would not be deductible from gross income because it is only ordinary *and* necessary expenses that are deductible.

►Can a doctor who, in treating a lacerated wrist, sutured one end of the median nerve to the sublimis tendon, be held liable even though there is no direct expert testimony that this constituted malpractice?◄

This question was passed on by the Supreme Judicial Court of Massachusetts in 1958 (*Fitzgerald* vs *Leach*, 150 N.E.(2d) 12). Plaintiff pushed her left hand through two panes of glass and suffered a laceration of her left wrist and flexor tendons. Defendant operated and plaintiff's hand was placed in a plaster splint and ace bandages for several weeks. After the cast was removed it was discovered that there was loss of median nerve function. An exploratory operation disclosed that the proximal segment of the median nerve was sutured to the distal portion of the sublimis tendon going to the middle finger. The distal end of the median nerve was found lying free. The condition was corrected.

A medical expert, who saw plaintiff shortly before the trial, testified she had some degree of recovery but still had a sensory loss at the base of the palm and a neuroma in her left wrist. He stated that the median nerve is approximately the same size as the sublimis tendon but its color is slightly different and that the sublimis tendon's texture is firmer than that of the median nerve which may be compressed with one's fingers. He testified that, in his opinion, so far as the median nerve is concerned the result of the operation performed by defendant was not good, that if the median nerve had been completely sutured instead of leaving one end lying loose, and that if one end of the median nerve had not been sutured to the sublimis tendon, the probabilities are that plaintiff would have obtained a better result from the operation. If the median nerve had been properly sutured she probably would not have suffered the neuroma which produced the sensory loss.

Defendant contended he could not be found guilty of malpractice because there was no direct medical testimony that he had not used the proper care and skill in treating plaintiff. The Court said the jury could reasonably find defendant negligent for failing to distinguish the sublimis tendon from the median nerve. It was implicit in the testimony of plaintiff's expert that the operation was not performed with the skill and care generally used in the community and that a doctor who operates in a field wherein nerves and tendons are exposed will distinguish them and not unite a nerve with a tendon.◄

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

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These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many business men. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

The combination of the highest interest rates in a generation and a heavy demand for loans should push banks' 1959 net operating earnings to record levels. New York bank stocks, in particular, appear especially attractive for moderate capital gains in an unusually safe industry. Reasons for their attractiveness at this time are the high interest rates on loans and Government obligations, the increase in interest rates on bank installment loans, and the good possibility of dividend increases. Furthermore, bank valuations at current levels do not appear to be excessive or to be discounting excellent earnings prospects.

The recent advance of the prime

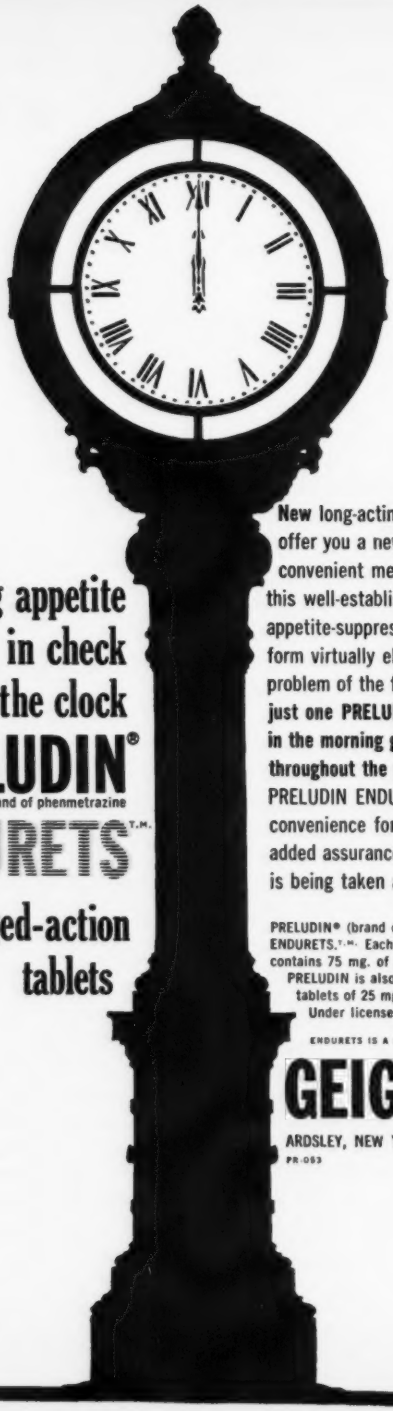
ite to 5% from 4½% was the third % increase since December 12, 958. This, when combined with the eneral tightening of "compensating alances" which now require a bor- ower to leave 15% to 20% of the an on deposit, plus heavy loan de- and should push gross earnings om loans and discounts up sharply. While the 40% increase in the "prime ate" over the past nine months is not et being fully reflected in earnings ecause of the normal time-lag in- olved in rolling over the loan port- olio, its effects became apparent in econd quarter statements. First uarter earnings for New York banks ere about the same as in the first uarter of 1958. However, second uarter earnings jumped 12% over he corresponding period of the previ- us year; third quarter earnings cored 15-20% gains and the fourth uarter will show another dramatic ncrease.

Also contributing to the rosy out- ook for New York bank stocks are he interest rates on Treasury bills nd other Government securities. J. S. Government securities in New ork bank portfolios as of June 30, 959, totaled $6.2 billion, or 17.6% of ssets, compared to $8.1 billion on June 30, 1958, when they comprised 22.1% of assets. Nevertheless, in spite of the sharp reduction in holdings of securities, income from securities climbed from $107 million in the first six months of 1958 to $126 million during the same period this year. Market yield on three-month Treas- ury bills went from .91% in July of 1958 to 2.82% in January, 1959, and continued upward to 3.20% in July, 1959; recent issues sold at close to 5%. Looking forward, it is possible to es- timate continued gains even on re- duced portfolios of Government se- curities.

Still another source of higher in- come yield is installment loans. New York banks—especially First Nation- al City and Manufacturers Trust— have in recent years been quite ag- gressive in developing this sort of business. The increase in interest rates, from 3¾% to 4¼% on se- cured loans and from 4¼% to 4¾% on unsecured, is the first such ad- vance in three years. Because of the much longer time-lag, the increase in this area has the function of a long-term factor.

Bank stocks this year have not par- ticipated to any great extent in the bull market. New York bank stocks as a group were virtually unchanged in the first quarter and up only about 6% in the second quarter. Since June 30th, they have declined about 4%, leaving the group very little higher for the year as a whole. Current market prices fix value of the last twelve months earnings at about 15 times and full year 1959 estimated at about 14 times. Dividends in the first six months represented a payout of 54% of net operating earnings, down from an average of 61% in 1958. Div- idend increases are a good possibility based on higher projected earnings and low present payouts.

This month we are discussing four New York bank issues. The stocks of all four banks are reasonably priced and possess a capital gains potential of 20-35% over the next twelve months. The banks under discussion are Chase Manhattan Bank, Chemi- cal Bank New York Trust, Irving Trust, and Manufacturers Trust Com- pany.



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Also contributing to the rosy outlook for New York bank stocks are the interest rates on Treasury bills and other Government securities. U. S. Government securities in New York bank portfolios as of June 30, 1959, totaled $6.2 billion, or 17.6% of assets, compared to $8.1 billion on June 30, 1958, when they comprised 22.1% of assets. Nevertheless, in spite of the sharp reduction in holdings of securities, income from securities climbed from $107 million in the first six months of 1958 to $126 million during the same period this year. Market yield on three-month Treasury bills went from .91% in July of 1958 to 2.82% in January, 1959, and continued upward to 3.20% in July, 1959; recent issues sold at close to 5%. Looking forward, it is possible to estimate continued gains even on reduced portfolios of Government securities.

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CHASE MANHATTAN BANK

Price	61
Dividend	$2.40
Yield	3.9%
Traded	O.T.C.

Capitalization (6/30/59)

Common stock ($12.50 par) ..... 13,167,000 shs.

THE CHASE MANHATTAN BANK

The largest bank in New York City, with over $8 billion in assets, Chase Manhattan Bank operates 103 offices in New York and 22 overseas, including 14 in the Caribbean area. Of these offices, four were acquired in the merger with Clinton Trust Company in January, 1959. A new branch, occupying five stories, was recently opened which will serve as midtown Manhattan headquarters for corporate customers. This will make the bank more readily accessible to the many large corporations located in that area. By late 1960, the bank's operations will be centered in its own 60-story building now under construction and costing a total of $133 million for the completed project.

As a result of its enormous size, Chase offers a diversity of banking services. Loans to small business and personal installment credit account for considerable volume; but by far the principal source of activity is loans to large corporations. The bank's operations in this area alone exceed those of any other bank in the United States. In 1958, income from loans produced 64% of the bank's gross. Investments in securities ranked second, accounting for 20% of income, and the remaining revenues came from trust fees, commissions, and other operations.

Chase Manhattan has also proven itself a leader in the areas of correspondent banking and trust operations. With access to over 51,000 banking locations throughout the world, it maintains a strong position in international banking functions. Trust services, incorporating extensive personal and corporate functions, round out the bank's activities.

As a result of rising interest rates and increased loan volume, earnings gains in recent years have been good. Over the years 1954-1958, the average rate on loans moved from 3.49% to 4.29%. Similarly, the average rates on securities rose from 1.85% to 2.45% during these years. Net operating earnings for 1958 edged up to $4.25 a share, against $4.24 a share the previous year.

For the current year, however, operating earnings are estimated to approximate $4.70 a share provided fourth quarter earnings fulfill expectations. During the first nine months of 1959, net operating earnings were $3.49 a share, up from the $3.16 for the corresponding period in 1958.

In recent years dividends have averaged approximately 56% of operating net. From 1954 to 1957, payments rose from $1.76 a share to $2.40. The $0.60 quarterly payment was continued in 1958, and prospects are good for an increase in the quarterly rate either late this year or in early 1960. If the dividend is raised, this will be the first increase since 1956.

CHEMICAL BANK NEW YORK TRUST

Price	59
Dividend	$2.40
Yield	4.0%
Traded	O.T.C.

Capitalization (6/30/59)

Common stock ($10 par) 8,476,590 shs.

As to the future earnings prospects of Chase Manhattan, the shares appear attractively priced, selling at 12.9 times estimated 1959 earnings of $4.70 a share. We recommend purchase of these top investment grade shares, which afford investors capital gains possibilities while offering a great deal of safety.

CHEMICAL BANK NEW YORK TRUST

The merger between Chemical Corn Exchange and New York Trust makes Chemical Bank New York Trust the third largest bank in New York City and fourth largest in the country. Shareholders of both banks voted in favor of the merger on July 8, 1959, and approval was made September 8, 1959, by the Superintendent of Banks of New York and the Federal Reserve Board. The merger increased Chemical's size by about 25%. From the standpoint of physical facilities, the move added seven branch offices to the system, boosting the total to 107. Six of the "new" offices are located in midtown Manhattan.

The merger increased the bank's deposits to $3.8 billion, compared to $7 billion each for the two largest banks in New York, Chase Manhattan and First National City. The combined total of capital funds is $338.7 million, thus augmenting the bank's lending capacity. This should attract more large industrial customers, as loans in excess of $33.8 million will now be available to any one borrower.

In addition to fiscal gain, the new bank acquired New York Trust's important industrial and correspondent bank customers as well as a nicely developed international business. A large trust operation, in particular personal trusts, will provide further new opportunities.

Under the merger, New York Trust shareholders received a total of 2,100,000 shares. Chemical Corn shareholders will continue to hold the same number of shares as before the merger. The book value of shares was diluted 3.2% from $47.37 as of June 30, 1959, to $45.86.

The consolidation with New York Trust represents the second merger effected by the organization since October, 1954, when Chemical Bank and Trust Company and Corn Exchange Bank Trust Company were brought together. The union of Chemical with a bank whose activities were primarily involved in a wholesale business enabled the new bank to commence operations with little duplication of customer accounts. However, corporate banking continues to be its chief concern. Chemical has also been active in fiduciary activities since the acquisition in 1948 of Continental Bank and Trust.

The principal factor contributing to Chemical Corn's rising income has been interest on loans. In 1958 more than 60% of the bank's gross income

IRVING TRUST

Price	39
Dividend	$1.60
Yield	4.1%
Traded	O.T.C.

Capitalization (6/30/59)

Common stock ($10 par) 5,202,000 shs.

was derived from this source. Following in second place was income from securities, accounting for 23% of the gross. The remainder of income accrued from trust fees, commissions, and other receipts.

During recent years the net operating earnings of Chemical Corn have been very stable. From $2.44 per share in 1954, the bank has steadily boosted earnings to $4.08 per share in 1958. For the 9 months of 1959, earnings rose to $3.41 a share, compared with $3.00 in the previous year.

Falling in line with earnings increase, the dividend climbed to $2.30 in 1958, against $1.92 in 1957. Under the new setup it is estimated that dividends will continue to be paid at the present $0.60 quarterly rate, as both members of the merger have a long record of uninterrupted dividends.

Basing predictions upon Chemical's above-average past record as well as its anticipated growth and economies in the future, Chemical Bank New York Trust appears to be a good buy at 12.4 times estimated 1959 earnings of $4.75. Selling at such a low-price earnings multiple, we consider the stock attractive for purchase.

IRVING TRUST

Irving Trust is one of the best-managed banks in New York, having compiled the best over-all record of any major New York bank since World War II. Its operations are well-balanced between retail and wholesale banking. Large trust and overseas banking departments also figure prominently in its activities. As an addition to its foreign program, a resident representative for Asia, with headquarters in Hong Kong, was appointed last year. The number of overseas companies for which Irving provides American Depository facilities increased to 40 during 1958. For its domestic operations, the bank set up a new department to handle trading in Federal funds.

On its various sources of earnings, loans rank highest, accounting for 60% of gross income in 1958. About 60% of these loans were commercial loans, 37% of which went to manufacturing and mining industries. In 1958, the average earnings on loans amounted to 4.16%. Securities were the second-largest earnings producer, drawing 24% of gross income last year. Trust fees, commissions, and rentals from the bank's 50-story head office building also contributed to income.

Net operating earnings maintained a firm course until 1950, when improved interest rates and higher-paying loans began to push earnings upward. By 1954, net operating earnings stood at $1.73 a share and rose steadily thereafter to a peak of $2.72 in 1957. Although earnings dropped to $2.59 in 1958, they are expected to reach a $3.05 high this year. Earnings

MANUFACTURERS TRUST COMPANY

Price	56
Dividend	$2.20
Yield	3.9%
Traded	O.T.C.

Capitalization (6/30/59)

Common stock ($20 par) 5,039,000 shs.

for the first 9 months rose to $2.08 from $1.90 in the same period last year.

Each year a portion of Irving's earnings are put into a general reserve. The bank either adds securities profits to or deducts losses from this reserve. As of June 30, 1959, the reserve totaled $2,843 million. In addition to this reserve, the bank held another $12.6 million to compensate for bed debts. This amount was not reflected in the balance sheet.

Since 1907, Irving Trust stockholders have been paid a dividend each year, and more recently 2% annual stock distributions have been made in addition to cash payments. The 1958 dividend totaled $1.57 a share, up three cents from the $1.54 of the previous year. Both the $0.40 quarterly dividend and the stock distribution are expected to continue.

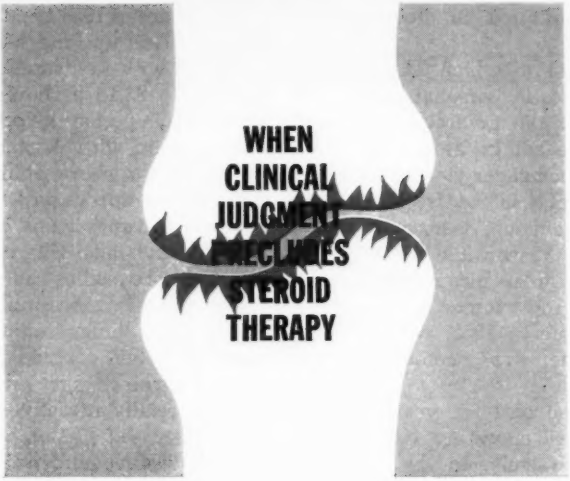
With New York bank stocks as a group selling at around 14 times estimated earnings, shares of Irving Trust appear to be an excellent buy at 12.8 times estimated 1959 earnings of $3.05. At this price it is obvious that investors are not paying a premium for the superior record and management of Irving.

MANUFACTURERS TRUST COMPANY

The sixth largest bank in the country with over $3 million in assets, Manufacturers Trust Company is New York City's largest retail or neighborhood bank. With 114 offices in New York City, its proportion of savings accounts deposits is the highest of the major banks, excepting U.S. Trust. While retail banking is the backbone of Manufacturers' operations, the bank is also active in "wholesale" operations, serving most of the large corporations in the country. The bank also maintains extensive correspondent relationships with over 2,000 banks throughout the United States. In the personal loan field Manufacturers is outranked only by First National City. International operations are conducted through branches in London, Tokyo, Rome and Frankfurt.

Continually seeking to expand and improve customer services, Manufacturers will soon open two new branch offices in New York City. Scheduled for occupancy late this year is a branch in the new Time-Life Building located in midtown. Space has also been leased for another midtown branch in a building now under construction.

Concurrent with the increase in merger activity among larger banks during 1958 and early 1959, Manufacturers considered a consolidation with Bankers Trust. However, no mutually agreeable terms for the move were turned up. Because the merger would have resulted in considerable duplication of branch offices at several locations, legislators and supervisors criticized the move. Discussions of the proposed merger



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Each ARTAMIDE tablet contains: Salicylamide 0.25 Gm. (4 gr.); Para-amino-benzoic Acid 0.25 Gm. (4 gr.); Ascorbic Acid 20.0 mg. (⅓ gr.); ORGANIDIN® (iodinated glycerol) 20.0 mg. (⅓ gr.).

DOSAGE: 2 tablets 3 or 4 times daily. Requirements may vary according to the response of the patient. SUPPLIED: ARTAMIDE Tablets, bottles of 100 and 500. REFERENCES: 1. Chambers, James O.: Clinical Medicine, 61:3 (1954) pp. 203-205. 2. Salter, W. T.: A Textbook of Pharmacology, p. 603, W. B. Saunders Co. (1952).

WRITE: Professional Service Department for literature and trial supply.

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were discontinued in February of this year.

The extent to which Manufacturers specializes in personal banking is reflected by the favorable return it draws on earnings assets. In 1958, loans and mortgages yielded an average return of 4.49%. Also the largest source of revenue, loans and mortgages were responsible for 56% of the bank's gross income last year. The second most important contributor to income in 1958, with 26% of gross income, was income from investments.

During the past ten years, Manufacturers net operating income has risen progressively. In the past five years, earnings have progressed from $2.94 a share in 1954 to a high of $4.07 in 1958. This uptrend has continued into 1959 with first nine-month earnings up to $3.42 a share from $2.95 for the same period the previous year.

This year, with earnings estimated at $4.75 a share, it is our guess that Manufacturers will show one of the best earnings gains of all major New York banks. Shares of Manufacturers are selling at one of the lowest price-earnings multiples of all banks—11.8 times estimated 1959 earnings. When coupled with the estimated earnings gain, this makes the stock especially attractive. Of the four stocks discussed, Manufacturers Trust Company is recommended as highly favored for purchase.◀

Declomycin Capsules *(Lederle)*

A new broad spectrum antibiotic. Each capsule contains 150 mg. of demethylchlortetracycline. *Indications:* Antimicrobial range is similar to tetracycline, but provides greater therapeutic effect with a lower dose. Provides sustained and longer antibacterial activity in the blood than tetracycline. *Dosage:* Adult dosage is 600 mg. daily, to be given 150 mg. four times daily or 300 mg. twice daily. Infants and children, according to body weight, divided into two or four doses. *Supplied:* In bottles containing 16 or 100 capsules.

Ilosone 125 Suspension *(Lilly)*

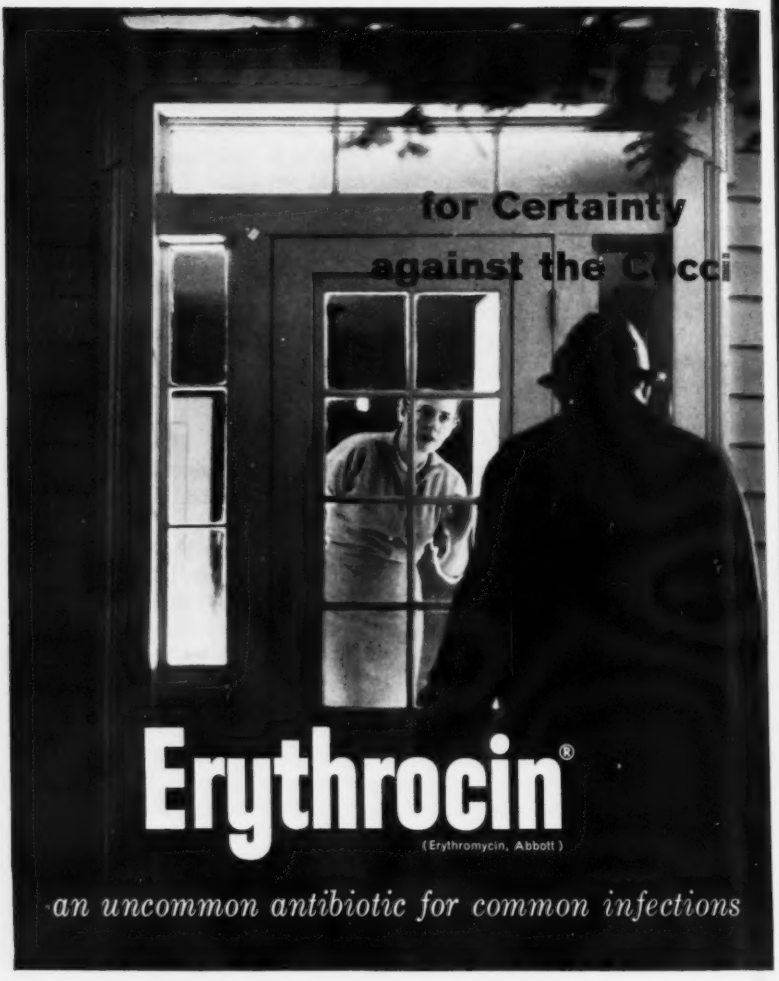
Each 5 cc. teaspoonful contains 125 mg. of propionyl erythromycin ester lauryl sulfate. For oral administration. *Indications:* For the treatment of infections caused by micro-organisms that are sensitive to its action (especially staphylococcus, hemolytic streptococcus and pneumococcus infections). *Dosage:* According to body weight and severity of the infection. *Supplied:* In bottles containing 60 cc. of suspension.

Midicel Tablets *(Parke, Davis)*

Each tablet contains 0.5 gm. of sulfamethoxypyridazine. *Indications:* For use in the treatment of bacterial infections. *Dosage:* Adults, in mild to moderately severe infections: 2 tablets the first day, then 1 tablet daily or 2 tablets every other day. In severe infections, 4 tablets the first day then 1 to 3 tablets daily, adjusted to the severity of infection and weight of the patient. Children, according to body weight and severity of infection. *Supplied:* In bottles containing 24, 100, 1000 or 5000 tablets.

Polaramine Expectorant *(Schering)*

Each 5 cc. teaspoonful contains 2 mg. of *Polaramine* maleate, 20 mg. of D-isoephedrine sulfate and 100 mg. of glyceryl guaiacolate. *Indications:* For relief of coughs and complications associated with allergic respiratory disorders. Combines antihistamine, decongestant, bronchodilator and expectorant action. *Dosage:* To be individualized according to patient's requirements and age. *Supplied:* In bottles containing 16 ounces or 1 gallon.



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Metrecal Powder *(Mead Johnson)*

Dietary for weight control. Contains protein, carbohydrate and fat, with added vitamins and minerals. *Indications:* To provide 900 measured calories for adequate nutrition with high satiety for overweight patients. May be used by patients of all ages. *Dosage:* One can (½ pound) of powder mixed with a quart of water makes 4 large glasses of beverage. One glass of beverage may be taken for each meal and one at bedtime. *Supplied:* In ½ pound cans, 3 cans per package.

AVC Vaginal Suppositories *(National Drug)*

New form. Each gelatin suppository contains 0.014 gm. of 9-aminoacridine hydrochloride, 1.05 gm. of sulfanilamide, 0.14 gm. of allantoin, with lactose added, buffered to an acid pH. *Indications:* For the treatment of all types of vaginitis including trichomonal leukorrhea, moniliasis, nonspecific vaginitis, cervicitis, post-partum hygiene, pre- and post-surgical treatment. *Dosage:* One suppository to be inserted twice daily. May be used during pregnancy. *Supplied:* Box of 12 suppositories with applicator.

Pro-Banthine Tablets (Half-Strength) *(Searle)*

New strength of the anticholinergic. Each tablet contains 7½ mg. of *Pro-Banthine. Indications:* Where lower dosage of the anticholinergic is required. *Dosage:* As determined by the physician. *Supplied:* In bottles containing 100 or 1000 tablets.

Terramycin Intramuscular Solution *(Pfizer)*

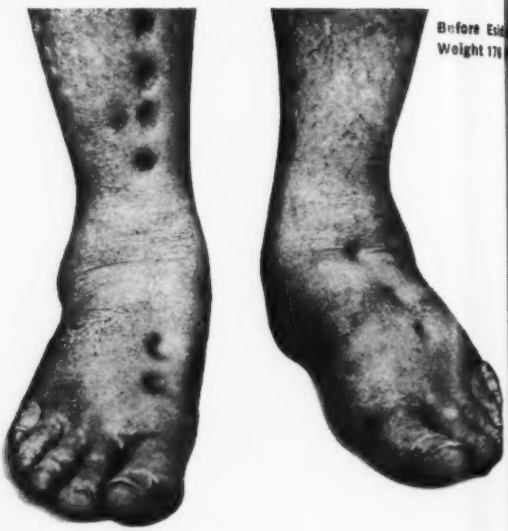
Formulation containing oxytetracycline and lidocaine in a stabilized liquid medium. *Indications:* For the treatment of common infections caused by susceptible organisms. *Dosage:* For intramuscular administration. Dosage depends upon type and severity of infection and the response of the patient. *Supplied:* Available in two strengths: Each 2 cc. ampul contains either 100 or 250 mg. of terramycin, each with the local anesthetic lidocaine, in a stabilized liquid medium. Either strength available in packages of 5 or 100 ampules.

Norflex Tablets *(Riker)*

Skeletal muscle relaxant. Each tablet contains 100 mg. of orphenadrine citrate. *Indications:* For any disorder in which skeletal muscle spasm is diagnosed and reduction of the spasm is desired. Acts to restore mobility to the affected muscle. *Dosage:* One tablet twice daily. *Supplied:* In bottles containing 50 tablets.

pantho-Foam *(U.S. Vitamin)*

Hydrocortisone 0.2% and pantothenylol 2.0% as an aerosol foam. *Indications:* For relief from pain, itching and inflammation in burns, traumatized lesions, stasis ulcers, atopic dermatitis, eczemas, neurodermatitis, contact dermatitis, poison ivy, pruritic lesions (anal, vulval, etc.). *Dosage:* Apply topically two to three times daily, or more often as needed. *Supplied:* In 2 ounce aerosol containers.



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pre-eminently effective whenever diuresis is desired

Indicated in: *congestive heart failure . . . nephrosis and nephritis . . . toxemia of pregnancy . . . premenstrual edema . . . edema of pregnancy . . . steroid-induced edema . . . edema of obesity*

Record of patient at a leading New York City Hospital. Photos used with permission of the patient.

Supplied: **Esidrix** *Tablets,* **25 mg. (pink, scored) and 50 mg. (yellow, scored); bottles of 100 and 1000.**

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The Preservation of Youth: Essays on Health

by Moses Ben Maimon (Maimonides), translated from the original Arabic (Fi Tadbir As-Sihha) and with an introduction by Hirsch L. Gordon, M.D., Ph.D., D.H.L. Philosophical Library, New York. 1958. $2.75

From your student days onward, you have heard frequent mention of Maimonides. The reading of this booklet will give you an accurate idea of the way his mind worked.

Early Diagnosis

edited by Henry Miller, M.D., F.R.C.P., Physician in Neurology, Royal Victoria Infirmary, Newcastle upon Tyne. The Williams and Wilkins Company, Baltimore. 1959. $6.50

How direct is the opening sentence: "The purpose of diagnosis is action; the purpose of early diagnosis is to institute as early as possible all measures which may be indicated for the cure, alleviation, and prevention of complications of the patient's illness, and for the protection of others." The eidtor, as you see, is a neurologist, among the 25 contributors are professors of surgery (general and special), of medicine, of child health, of psychological medicine, and general practitioners. You may take the book on trust, as one of unusual value in your daily practice.

Clinical Dermatology for Students and Practitioners

by Harry M. Robinson, Jr., M.D., Professor of Dermatology and Head of the Division of Dermatology, University of Maryland School of Medicine; and Raymond C. V. Robinson, M.D., M.Sc. (Med.), Associate Professor of Dermatology, University of Maryland School of Medicine. The Williams and Wilkins Company, Baltimore. 1959

It is recognized that frequently the first clue to the nature of the underlying disease is afforded to the eye that will closely inspect and the mind that will accurately interpret lesions shown on the skin, and that in many cases skin abnormalities subjected to analysis will clarify puzzling disorders of various kinds. This text draws from vast clinical experience and is

intended primarily for the medical student, but will serve well the general practitioner and any specialist in the healing art. The illustrations vividly supplement the text. Many charts and tables simplify differential diagnoses and laboratory and management methods.

The Sedimentation Rate of Human Erythrocytes: Its Basic Concepts; Its Value as a Differential Diagnostic Agent; Its Multiple Clinical Applications

by Frank Wright, M.D., F.A.C.P., F.A.S. Vantage Press, New York, Washington, Chicago, Hollywood. 1958. $2.50

The author, one of the most learned of physicians and medical scientists, has provided this book to emphasize the great value of the ESR. He discusses its basic concept, its value as a differential diagnostic agent, and its multiple clinical application. Even should it turn out that the ESR will not do all this enthusiastic scholar-doctor believes it will, if it will do half as much, great good for your patients will result.

Ciba Foundation Symposium on Carcinogenesis: Mechanisms of Action

editors for the Ciba Foundation G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Maeve O'Connor, B.A. With 48 illustrations. Little, Brown and Company, Boston. $9.50

Just before the 7th International Cancer Congress in London in 1958, a Symposium on Carcinogenesis was held. The complete record of the Proceedings is here presented. The various theories of carcinogenesis, methods of inducing tumor growths, considerations of possible two-stage mechanisms, hormonal carcinogenesis, pharmacological approach, immunology, relation of protein binding, biochemical induction of bladder cancer, the nature of the neoplastic transformation in lymphoid tumor induction, the possible role of metals—all these are included in the many aspects of the subject, all exhaustively dealt with by those most learned in the subject.

A Textbook of Medicine

edited by Russell L. Cecil, M.D., Sc.D., Professor of Clinical Medicine Emeritus, Cornell University; Robert F. Loeb, M.D., Sc.D., D. Hon. Causa., LL.D. and Associate Editors; 10th edition. W. B. Saunders Company, Philadelphia & London. 1959. $16.50; also in two volumes—Vol. 1 contains pages 1 through 773, illustrations—figures 1/86; Vol. II contains pages 774 through 1665, illustrations—figures 87/182. Price of the 2 volumes, $20.50

It is always a pleasure to welcome a new edition of the Textbook of Medicine, the first edition of which was the work of Dr. Russell L. Cecil. The present, 10th, edition is the joint work of some 175 authorities. It is astonishing how successfully the essentials of the internal medicine of today have been set forth in one volume. The admirable text is complemented by an excellent index. The authors are to be congratulated for having made this work available, the purchasers and readers on having it made available for them.

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REFERENCES: 1. Brit. M. J. 1:407, 1952. 2. Bull. Margaret Hague Mat. Hosp. 1:68, 1948. 3. Am. J. Obst. & Gyn. 57:541, 1949. 4. Connecticut M. J. 14:930, 1950. 5. J. Lancet 66:218, 1946. 6. Am. J. Obst. & Gyn. 62:947, 1951. 7. Am. J. Med. Sc. 212:76, 1946. 8. Obst. & Gyn. 5:201, 1955. 9. J. Ped. 41:170, 1952. 10. Pennsylvania M. J. 51:999, 1948. 11. Ann. Int. Med. 42:458, 1955.